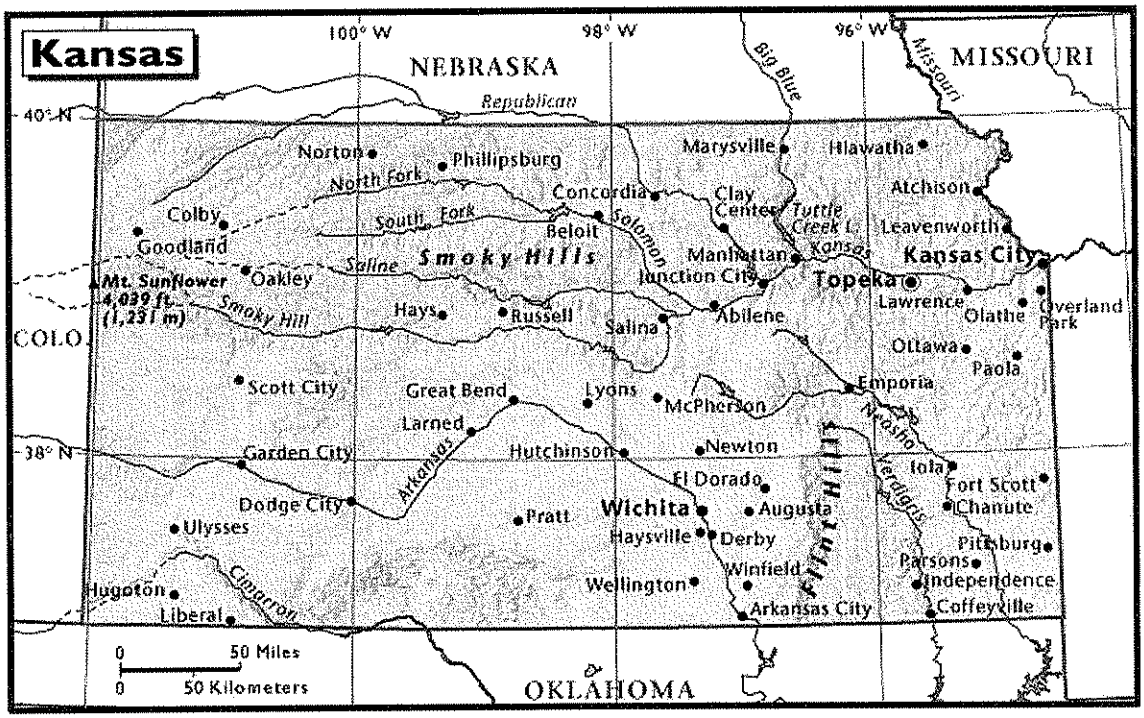
CONSULTATION REPORT

KANSAS

NEWBORN SCREENING PROGRAM

August 15-17, 2005



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CONSULTATION REPORT
KANSAS NEWBORN SCREENING PROGRAM

1.0.0 Executive Summary

The following brief outline presents summary information outlined in more detail within the written report that follows. The points outlined here are meant only to provide a quick glance at the report and should not be taken out of context without viewing the supporting information in the report. Reference materials are included in the Appendices to aid the reader in achieving a fuller understanding of some of the issues discussed. In order to better understand the broad concepts of newborn screening (NBS) as a system that includes the public health program as one component, attention should be paid to Appendix 3 [*U. S. Newborn Screening System Guidelines: Statement of the Council of Regional Networks for Genetic Services (CORN).* Screening 1992;1:135-147.] and Appendix 4 [Executive Summary - *Serving the Family from Birth to the Medical Home: Newborn Screening a Blueprint for the Future.* Pediatrics 2000;106(suppl 2):383-427].

1.1.0 Legislation

- The current Kansas NBS statute defines 3 conditions for inclusion and allows for inclusion of others: "phenylketonuria, galactosemia, [congenital] hypothyroidism and such other diseases as may be appropriately detected on the same specimen." (The latter category of diseases is currently limited to sickle cell diseases.)
- The legislation allows for an education, follow-up, and case registry program with testing at no charge "by the department of health and environment for all infants born in the state."
- Kansas is currently one of 7 states that does not provide expanded NBS using tandem mass spectrometry (MS/MS) technology, and several of the 7 will soon be expanding (Kansas statutes allow for expanding NBS through tandem mass or other technology).
- Kansas is one five states that does not charge a fee for NBS as a means of recovering part or all of NBS costs. (Kansas statutes do not include a NBS fee).
- Kansas is one of a very few states that pays for treatment of conditions identified through NBS. While laudable, financial support for treatment likely results in restrictions for testing and will be difficult (or impossible) to adequately sustain if expanded screening is to occur. (Most programs pay for portions of treatment expense based on a sliding fee scale related to family income.)

1.2.0 Scope of Responsibility

- Procedure manuals documenting laboratory responsibilities and procedures, with procedures in place for ongoing review, are available at the State NBS Laboratory.
- Procedural manuals documenting follow-up/education responsibilities and procedures, with procedures in place for ongoing review, are not available for NBS nursing follow-up.

- A NBS policy/practitioner manual is currently under review and will be disseminated defining other responsibilities within the program.

1.3.0 Advisory Committees

- Outside advice from a group of NBS stakeholders can provide invaluable information and advocacy for the program. While health and medical professionals should be a part of the group, others (patients and families, insurers, hospital administrators, advocacy groups, etc.) should also be involved. [This is particularly important given the rapidly changing environment of NBS -- the Kansas Department of Health and Environment (KDHE) should play a support role]. This does not preclude the need for an internal working group to guide routine program operations.
- The Advisory Committee should have written bylaws defining its mission, member responsibilities, communication procedures to KDHE, and scope of input (policy matters, system components, screening protocols, scope of tests, etc
- Program financing considerations should include funding to support the Advisory Committee.
- The Kansas Newborn Screening Program (KNSP) needs to strengthen family involvement in the NBS program.

1.4.0 Program Centralization

- For maximum program efficiency, the KNSP should have a strong centralized administrative staff and central data repository.
- An integrated child health information system will facilitate NBS follow-up, management/intervention, and evaluation activities. Presently there are separate (and somewhat duplicative) systems for the NBS laboratory, NBS follow-up, hearing screening, and Children with Special Health Care Needs). Data system integration with vital records will ensure that all Kansas newborns receive a newborn screen. .
- NBS laboratory services are most efficient when tests exceed 30,000 annually. A single MS/MS instrument can analyze approximately 100,000 specimens annually. Thus, with approximately 37,000 annual births, the KNSP may find it more efficient to consider participation in a regional MS/MS testing program.

1.5.0 Evaluation and Selection of Conditions for NBS

- A logical, scientific and informed process for evaluating and selecting conditions to be included in the Kansas NBS panel needs to be delineated.
- A decision matrix has recently been described by the American College of Medical Genetics (ACMG), which should be considered for use in screening considerations in Kansas.
- The recently released recommendations for a core panel of conditions accompanied by determination of certain secondary conditions should be strongly considered for adoption in the KNSP.

1.6.0 Laboratory Considerations

- Analytical methods and quality control appear to exist in the KNSP laboratory such that disease detection is maximized with minimal false positive and false negative screening test results.
- Expansion of the KNSP using the existing NBS laboratory will likely require up to 3 additional persons, depending on methodologies adopted for testing.
- The KDHE laboratory appears to have adequate facilities and infrastructure to accommodate expansion of the mandatory testing, although some renovations will likely be needed . If the laboratory is outsourced, then a back-up plan would be needed in case of difficulties with the laboratory providing the services. If the public health laboratory were to discontinue screening services, it would be unlikely that it could ever be restarted without a large expenditure and increased staffing.
- Expanded testing to include MS/MS and other conditions would likely require a start-up time of at least 6 months, possibly 9-12 months to allow purchase or lease of equipment, recruitment of personnel, training, protocol development, and dissemination of educational information.
- Expanded testing would likely include conditions for which rapid test result turnaround is essential to avoid negative consequences. A 6-day or 7-day workweek should be considered to ensure best patient outcomes.
- Equipment for MS/MS testing can be purchased or leased. A single MS/MS instrument would cost approximately $200,000 and could be lease/purchased over a 5-yr period. A back-up plan in conjunction with another state laboratory is needed to ensure operation when down time is encountered.
- A courier system would likely improve transit times for specimens from collection to testing.
- Laboratory services for confirmatory testing for each group of conditions should be identified by the Advisory Committee and provided to primary care physicians and subspecialists as part of the follow-up confirmatory process.

1.7.0 Follow-up Considerations

- The current follow-up system appears to be effective in resolving all presumptive positive screening results, but evaluation of timeliness and outcomes are lacking.
- The follow-up data system should be able to track performance measures such as time to diagnosis, treatment compliance, and periodic assessments of outcome for program evaluation and improvement. Other performance indicators should be considered (see Performance Evaluation and Assessment Scheme (PEAS) available at http://genes-r-us.uthscsa.edu.
- NBS expansion in Kansas would probably require at least one new follow-up nurse, one data person and an overall NBS Program Director; depending on the number of conditions included in the screening program (investigate models in other states with similar screening programs such as Nebraska or Oklahoma).
- Long-term follow-up is essential for determining ultimate program value and for assisting patients in obtaining related services. Long-term follow-up is lacking in the KNSP and should be considered as program changes are contemplated.

1.8.0 Documentation

- Result reporting and follow-up activities appear to be documented, but no formalized mechanism for evaluating the documentation for program improvement is in place.
- If a courier system is instituted, birthing centers should be instructed to document specimen pick-up.
- Birthing centers should be included in an education plan that encourages identification of newborn's medical home and documented receipt of screening results on all patients and actions in response to recommendations from the KNSP.

1.9.0 Computerization

- A data integration plan should be developed that includes consideration of all child health information systems including NBS laboratory, NBS and hearing follow-up, immunizations, vital registries, CHSCN, etc.
- The laboratory collection device serial number should be strongly considered as a linking number for database integration or linkage. The format for the serial number should conform to NCCLS/CLSI recommendations (see NCCLS/CLSI LA4-A4).

1.10.0 Education

- A comprehensive education plan should be developed that includes education for newborn screening staff, consumers, health professionals, birthing facility staff, and policy makers.
- Limited education of birthing center staffs has been accomplished by the screening laboratory as needed, but a formal system of ongoing education does not appear to be in place.
- A meaningful education program may require a dedicated staff person or integration with other educational programs reaching similar audiences.
- The CSHCN contracts with subspecialty providers should include an education component and this should be continued and evaluated to ensure that it is working.

1.11.0 Quality Assurance

- The screening laboratory has appropriate quality assurance procedures in place as part of its CLIA certification.
- Quality assurance should extend beyond the laboratory. Indicators of appropriate quality should be selected in consultation with the Advisory Committee and monitored on a periodic basis sufficient to provide for meaningful evaluation.
- The current rate of approximately 6% of specimens deemed unsatisfactory is high and should be targeted for improvement – submitter education is a likely means of improvement.
- Birthing center procedures for collecting and submitting specimens may not be correct, including removal of specimen card 'flaps' designed to comply with US Postal regulations, and collection procedures should be a part of ongoing education

provided by the KNSP.

- Assignment of a quality assurance officer or assigning specific quality assurance responsibilities to appropriate staff members should be strongly considered.

1.12.0 Treatment

- Kansas does not have a statute that requires insurers doing business in the State to cover metabolic foods and formulas considered medically necessary for treatment of metabolic conditions identified through NBS. Examples of such legislation may be obtained from other states.
- Medicaid regulations allow for screening and treatment coverage as a part of NBS, and such coverage has recently become an item for consideration in Kansas.
- Treatment guidance should be a consideration of the Advisory Committee. The ACMG will soon make available to States materials for distribution to primary care providers outlining immediate next steps to take following receipt of a positive NBS result. KNSP should consider customizing the materials for use by the program.
- Treatment cost estimates should be developed in cooperation with the Advisory Committee. Comparative treatment costs are available from other sources; particularly the Wisconsin program and published articles (see Appendix).

1.13.0 Funding

- Medicaid reimbursement for NBS testing appears to be available for laboratory equipment purchases, but does not appear to have been used for other program costs related to patient testing.
- In order to pay for expanded screening, a fee-based system will likely be necessary. The most popular fee mechanism is through advance sale of specimen collection cards to birthing facilities. Fee funds should be dedicated to NBS program expenses, which should be comprehensively evaluated. A preliminary fee estimate of $70/newborn was provided to the Review Team to cover screening, follow-up, education, data management, etc. for the 29 core conditions and 25 secondary targets listed by the ACMG (which excludes hearing screening).
- Fees may be recovered by other mechanisms such as billing birthing facilities, but sale of collection kits is simpler. Fees have to take into account those patients who cannot pay.
- The local March of Dimes Chapter represents a possible mechanism for funding Advisory Committee activities if State funding is not available.
- Financing considerations should be discussed with stakeholders, including third party payers, birthing facilities, medical care providers, etc.
- Appropriate accounting records should be maintained such that total program costs can be calculated including costs of confirmatory testing and medical care. In this way cost benefit calculations may be made in order to assess program benefit.

1.14.0 Consultant Resources

- The number of pediatric subspecialists available to work with conditions identified

through an expanded NBS program is likely insufficient within the State, particularly for metabolic conditions.

- Available subspecialists appear supportive and interested in the KNSP and 3 of 6 subspecialists participated in the meetings with the Review Team. About 10 physicians attended a meeting with the Review Team at Kansas University Medical Center.
- Kansas may need to partner with Missouri and/or Nebraska to have the breadth of consultation needed to expand NBS.
- Opportunities for small grants and other collaborations may exist in the HRSA-funded regional collaborative (Heartland Genetics Consortium).

1.15.0 Liability

- Lawsuits have been filed in other states when newborns have been affected by conditions that might have been included in screening programs but were not.
- Lawsuits have affected hospitals that did not inform parents of newborns that testing for conditions not included in the state mandate were available from other sources in instances where a newborn is adversely affected by a condition that could have been screened and was not.
- Lawsuits have included state NBS programs in instances where written procedures may not have been followed either in the laboratory or in the follow-up program.
- Lawsuits have included couriers, hospitals and screening laboratories relative to the chain-of-custody of specimens.
- Documentation of all actions associated with a particular specimen/newborn are important to reduce legal exposure. This includes all actions from the point of collection throughout the newborn screening process including diagnosis and treatment.
- Specimens represent a potential source of information about screening tests for approximately 6 months. Beyond 6 months, they are potential sources of research due to the availability of DNA. Written protocols should exist defining the procedures for retention, storage, and use of NBS specimens (see NCCLS/CLSI LA4-A4 for recommendations about storage conditions. The Advisory Committee and legal counsel for the KDHE should be involved in specimen storage policies.

2.0.0 Introduction and Background

2.1.0 Logistics Summary

On August 15-17, 2005 a select Newborn Screening Technical Assistance Review Team (Review Team - brief resumes in Appendix 1) reviewed the newborn screening program of the Kansas Department of Health and Environment (KDHE). The review service is sponsored by the National Newborn Screening and Genetics Resource Center (NNSGRC) through a cooperative agreement with the Genetic Services Branch of the Maternal and Child Health Bureau (MCHB), Health Resources and Services Administration (HRSA). This review was at the request and joint invitation of Roderick Bremby, Secretary, KDHE and Linda Kenney, MPH, Director, Bureau for Children,

Youth and Families. In addition to meeting with personnel associated with the administration and follow-up components of the Kansas Newborn Screening Program (KNSP) housed at the Curtis Building, the Review Team visited the newborn screening laboratory facilities at Forbes Field and the follow-up/administrative facilities at the Curtis Building. The Review Team also met with representatives of the laboratory and maternity sections at the Stormont-Vail Hospital in Topeka, participated in a videoconference session at the KDHE office facility, and met with advisory committee members and other program stakeholders at the Kansas University Medical Center in Kansas City. An oral exit review was held with interested staff and stakeholders at the conclusion of the visit and a debriefing meeting was also held with Dr. Howard Rodenberg, State Health Officer.

2.2.0 Logistics Details

Participants at the initial overview session on August 15 included: from KDHE – Roderick Bremby (Secretary), Dr. Howard Rodenberg (Director of Health), Linda Kenney (Maternal and Child Health), Jamey Kendall [Children with Special Health Care Needs (CSHCN)], Carolyn Nelson, Melanie Warren (KNSP Follow-up Coordinator), Greta Hamm (Medicaid) and Willie Craft (KNSP Laboratory); family adovocates – Michelle and Bill Leeker and their son, Zac Leeker; KNSP medical advisor – Dr. Leona Therou; March of Dimes Birth Defects Foundation representative – Steve Kearney; insurance representative William Pankey (First Guard Health Plan); and hospital representative Deborah Stern [Kansas Hospital Association (KHA)]. Following welcome and introductory comments from Mr. Bremby and Dr. Rodenburg, Mr. Craft (KNSP lab) and Ms. Warren (KNSP follow-up) provided details on the program and Ms. Jamie Kendall spoke about the CSHCN program. Mr. and Mrs. Leeker then commented on program expansion, strongly expressing the need for expansion to prevent future deaths from screenable diseases and the hope that expansion and research would eventually lead to screening for Krabbe Disease, which caused the death of their child.

A videoconferencing session allowed discussions with stakeholders who were unable to journey to Topeka. Participants included KDHE staff members Linda Kenney, Melanie Warren, Jamey Kendall, and Carolyn Nelson, and KNSP medical consultants Leona Therou, M.D. and Robert Trueworthy, M.D. This session included brief discussions of the Children with Special Healthcare Needs (CSHCN) Program, Newborn Hearing Screening and issues raised by the consultants to the program. Issues discussed included the need for better data from the KNSP for the advisory group, the need for a more formal committee structure, and concern about insurance payments for children identified with an untreatable condition through expanded screening. Also noted was the fact that information about the hemoglobinopathy reference services available at the Children's Hospital at Oakland Research Institute (CHORI) was not widely known. There was an expressed need to review newborn screening legislation from other programs.

On August 16, a meeting was held with interested stakeholders at the KU Medical Center including: R.N. Schimke, M.D.(clinical geneticist), Debra Collins, M.S. (genetic counselor), Kathy Ellerbeck, M.D. (developmental pediatrician), Chet Johnson, M.D.

(Director, KU Developmental Disabilities Center, and Chair, Department of Pediatrics), Leona Therou, M.D., (pediatrician - PKU medical advisor) James Casey, M.D. (pediatric endocrinologist), Carole Prather, R. N. (family nurse practitioner), Adrienne Lieberger, R. N. (cystic fibrosis nursing coordinator), Norm Hess (March of Dimes Director of Program Services), and Michelle Leeker (parent of deceased child with Krabbe Disease). Accompanying the Review Team to the meeting were KDHE staff members: Willie Craft, Linda Kenney, Jamey Kendall, Melanie Warren, and Carolyn Nelson. In addition to discussions on various conditions being considered for expansion, there was also discussion on the logistics of follow-up including interactions with subspecialists in Missouri. Other out-of-state professional relationships were discussed including possible interactions with Dr. Schaefer and Dr. Lutz in Nebraska.

The Review Team, along with some members of the KDHE staff (Willie Craft, Melanie Warren, Jamey Kendall, and Carolyn Nelson), also visited Topeka's Stormont-Vail Hospital. Jeff Anderson provided an explanation of laboratory activities related to newborn screening. He noted that the hospital owns two copies of the CLSI video on newborn screening specimen collection and that specimens are sent to the KNSP laboratory three times weekly. Amy Spurgeon-Hocher, nurse supervisor, provided a description of maternity activities related to screening, and Joy Carlson and other staff members from the intensive care nursery provided additional input. Of major concern was the fact that specimens collected and submitted from Stormont-Vail Hospital did not contain the flap over the blood spot end of the collection form, which is provided to meet postal regulations regarding double packaging. Further investigation revealed that the laboratory receiving area at the KDHE was aware of incoming forms with missing flaps, but had taken no actions to resolve the situation.

At the exit meeting on August 17, the Review Team reviewed the questions posed to the group as well as other issues encountered during the visit. Attending this review, in which a verbal summation of this report was presented, included: Linda Kenney, Melanie Warren, Carolyn Nelson, Jamey Kendall, Greta Hamm, Dr. Duane Boline (KDHE, Director of Health and Environmental Laboratories), Willie Craft, and Norm Hess. Team members discussed each of the issues and provided suggestions concerning possible future actions to improve the various situations reviewed.

The Review Team was impressed with the cooperation of all personnel with whom it interacted, both at the KDHE and at the other facilities. The program staff appears dedicated and interested in maintaining a successful, effective newborn screening program as evidenced by their involvement in this review. The Review Team was particularly impressed with the attention to customer service given by Mr. Craft in the laboratory, and the attention given to providing for the medical needs of patients through the current program and departmental financing scheme. By the same token, the Review Team recognizes that the KNSP currently offers a less comprehensive testing program when compared to other programs around the country. The dedication of all staff associated with the screening program and KDHE administration's interest in providing a quality newborn screening program that meets the needs of Kansas citizens was evident.

2.3.0 State Overview

Kansas is a rectangular state measuring 208 by 411 miles. It rises from less than 700 feet above sea level in the southeastern corner to more than 4,100 feet at the western border and contains a total of 82,264 square miles. Kansas is 14th in geographic size among the states. Because of the distance from east to west, Kansas has a large variation in climate, terrain, soil and native plants, and animals. Most of the state lies within the Great Plains region of the country, and the economy is dominated by the aircraft industry and agriculture related enterprises. Kansas is the world leader in producing general aviation aircraft, and more than 30,000 workers are employed by four major aerospace companies. There are 34,000 farms with cattle, making Kansas the second leading beef processor in the United States. Unemployment in Kansas is consistently among the lowest in the nation. Kansas state government is based in Topeka, which has served as the state capital since Kansas became the 34th state on January 29, 1861.

Kansas is one of the few states that does not issue revenue bonds to finance general government activities. A "cash-basis law" requires that the state operate strictly on the money available. Bond issues are allowed for capital improvements, such as major roads and buildings. With a health indicator score 5.8 % above the national norm, Kansas was ranked as the 23rd healthiest state, by the *America's Health: State Health Rankings—2005 Edition (*a joint effort of the United Health Foundation, the American Public Health Association and Partnership for Prevention). Kansas ranked as the 16th healthiest state in 2004. Strengths include a low rate of uninsured population at 11.1 percent and a low incidence of infectious disease at 8.5 cases per 100,000 population. Challenges include low immunization coverage with only 77.5 percent of children ages 19 to 35 months receiving complete immunizations, low per capita public health spending at $95 per person, and an increase in the percent of children under age 18 in poverty from 14.5 percent to 15.6 percent. In 2003-2004, 11.5% of the population was covered by Medicaid. Approximately 57% of the Medicaid recipients were children. There is also a wide disparity in the infant mortality rate, which varies from a low of 6.4 deaths per 1,000 live births for non-Hispanic whites, to a high of 14.7 deaths for non-Hispanic blacks.

Information in the *Maternal and Child Health 5 -Year Needs Assessment (2005)* (http://www.kdheks.gov/bcyf/download/mch_2010.pdf) provides the following Kansas health statistics:

- *In 2002, 86.1% of pregnant women started prenatal care in the first trimester of pregnancy. This is slightly higher than the national rate of 82.1%, but below the Healthy People 2010 goal of 90%. Hispanics, African-Americans, and teens had disproportionately lower rates. Black and Hispanic rates were 78.9% and 71.1% respectively. Geographically, early prenatal care rates are lowest in Southwest Kansas.*

- *Nationally and in Kansas, low birthweight rates increased slightly over the past decade. The 2002 rate for Kansas, 7.0 per 1,000 live births, was slightly lower than the national average of 7.8 but above*

the Healthy People 2010 goal of 5.0. African American low birthweight rates remained disproportionately high at 12.4 per 1,000 births.

- *Nationally and in Kansas, the rates of pre-term births (less than 37 weeks gestation) increased slightly over the past decade. Kansas performed better than the national rate, with a rate of 8.6 per 1,000 live births versus 12.1 for the U.S. (2002). The Kansas African-American rate of 12.3 was substantially higher than that for other groups.*

2.4.0 Newborn Screening Program Information

Screening for phenylketonuria (PKU) was mandated in Kansas in 1965. The law was amended to include testing for congenital hypothyroidism in 1977 and galactosemia in 1984. Hemoglobinopathy screening on request began in 1990 and in 1993 it was mandated for all newborns. Under State law, it is the responsibility of the person in charge of the hospital, birthing facility, or the attending physician to provide an appropriate blood specimen for PKU, hypothyroidism, galactosemia, and hemoglobin screening on all infants in their care.

There are approximately 37,000 births annually with 60% of the births occurring in 10 birthing facilities. The number of out-of-hospital/birthing facility births is not known. Approximately 93% of all births are recorded via electronic birth certificates. There is no state plan for further comprehensive public health program computerization. While there is currently no newborn screening fee in Kansas, a matching algorithm is used to identify Medicaid covered babies (approximately one-third of all Kansas births) whose specimen testing is eligible for coverage with laboratory reimbursement at approximately $34 for each. The program is primarily funded with general revenue funds. With current consideration given to expanding screening to include the 29 conditions identified in a core screening panel by the American College of Medical Genetics (ACMG), a fee is under discussion as a way to offset the expenses of program expansion.

Table 1 on the following page was created from information supplied to the Review Team from the NNSGRC. These data are data reported by the KNSP to the national NBS database and validated by the submitter. They give an indication of the success of Kansas's screening program in terms of cases detected.

Table 1. Kansas Newborn Screening Summation 1991-2000

Year	Births[1]	PKU	CH	GAL	FS	FSC	FSA	FAS
1991	36,452	1	7	1	7	1	NA	171
1992	36,500	2	8	0	1	1	5	225
1993	35,850	1	11	0	2	1	1	316
1994	35,798	3	10	3	4	5	7	319
1995	35,527	4	14	1	12	4	1	257
1996	35,360	4	9	1	6	1	5	272
1997	36,050	4	13	2	6	0	3	296
1998	37,450	1	8	2	3	2	0	246
1999	38,231	4	15	0	5	5	5	315
2000	39,248	1	39	1	0	2	1	324
Totals	366,466	25	134	11	46	22	28	2,741
Incidence	--	1:14,659	1:2,735	1:33,315	1:7,967	1:16,658	1:1.786*	1:134

[1] From National Center from Health Statistics

*Calculated using 330,014 births (omitting 1991 data)

The KNSP laboratory staff currently includes 6 professional personnel, exclusive of the data entry staff, who are in a separate unit. Testing in the laboratory occurs 5 days/week from 8 am – 5 pm. There is a Kansas practitioner manual that is currently being updated and reformatted for publication on the Internet.

The KNSP laboratory receives approximately 46,500 specimens annually (the number of specimens is much greater than the number of births because some pediatric practices routinely obtain a second specimen at the first outpatient visit and one hospital obtains a second specimen at newborn's day 3 or 4 of life.) Approximately 10% of the specimens received are transported by courier with the remainder arriving via US Mail. Bar coded serial numbers are linked to birthing facilities receiving the forms such that an inventory system is maintained and used for automatic input of submitter identifying information at the time of data entry. Phone calls are made to submitters in order to identify the newborn's physician on all specimens arriving without this information. Reports of laboratory results are provided to both the birthing facility and the physician identified on the submission form. For submitters with fax numbers on file, reports are automatically faxed, with the result that approximately 60% of all reports are faxed. Most laboratory reports are finalized and submitted within two days of specimen receipt. Subsequent specimens are linked to initials specimens using an algorithm that includes mother name, social security number and other identifying information. A monthly quality assurance report is generated from the screening laboratory identifying the number of unsatisfactory specimens received and other critical information for each specimen submitted. The laboratory owns copies of the CLSI/NCCLS videotape on specimen collection on filter paper, and these are available for loan to specimen submitters. The newborn screening laboratory director visits hospitals requesting educational assistance. All residual blood specimens are retained at -20 degrees C for one month and are then autoclaved and destroyed except for abnormal specimen cards which are retained indefinitely.

The KNSP follow-up system consists of a single nurse coordinator, Melanie

Warren, and an administrative assistant. Six medical consultants (2 endocrinologists, 2 hematologists, 1 PKU specialist, and 1 galactosemia specialist) are available to the program through contracts to provide follow-up and management and all (in addition to others) serve as program advisors. Follow-up contact with physicians is a responsibility of the follow-up nurse. Upon receipt of presumptive positives from the lab each morning she telephones the appropriate medical consultant the screening reports determined to be at high risk for a condition (presumed positive) including abnormal hemoglobinopathies. Hemoglobin carriers are not telephoned, but instead receive a letter from the program. In addition to the laboratory staff mailing or faxing all abnormal findings to the appropriate primary care physicians, the follow-up nurse sends letters to the parents and physicians of all newborns who are presumed positives. Borderline results for PKU and GAL are telephoned to the physician identified on the screening form as well. Computerized files remind the follow-up coordinator of specimens requiring additional follow-up at one month following the initial contacts. Notification/reminder letters are then sent and again at 60 days, if necessary. Cases are kept open until diagnosis is confirmed. Newborns in the Kansas City area may choose to be seen by physicians and subspecialists in Missouri for convenience or some premature infants may be transferred to Missouri tertiary care centers and these scenarios present a special challenge in terms of follow-up. The follow-up data system is a part of the CSHCN Program, unlinked and separate from the lab database, and does not include disease carriers.

The CSHCN program resides in the Bureau for Children, Youth, and Families, as does the KNSP follow-up program and is responsible for medical management for children identified with the four required screening conditions and maple syrup urine disease (the latter specifically required in the statute). It contracts with medical consultants (there is one geneticist; no board certified metabolic geneticist in the state) to provide clinical and diagnostic services. The consultants submit quarterly statistical reports to CSHCN. Metabolic formula is supplied to each patient at no charge. In July 2004, the formula distribution system changed from a central pharmacy to a system of direct ordering from the manufacturer. The distribution of synthroid to CH patients occurs through local pharmacies, which receive reimbursement for the synthroid. No financial criteria exist for receiving treatment supplies for CH, PKU or GAL, although families must reapply for services annually. Medicaid funding is not currently a part of this program and this will likely change in the near future. Low protein foods are also provided for families up to 300% of the federal poverty level until 18 years of age, with a maximum expenditure of $1500 annually per patient. Penicillin prophylaxis is also provided for sickle cell disease patients with a financial requirement that the family income must not exceed 185% of the Federal poverty level.

2.5.0 Organization of Consultation Report

This Consultation Report is organized to first address the specific areas of concern raised in the invitation from Secretary Bremby and Ms. Kenney. Section 2 contains answers to these concerns. Section 3 includes discussions of other points considered important by the Review Team. Finally, Section 4 includes an overview summation using a template in which strengths, weaknesses and possible future actions are enumerated. This overview takes the place of an executive summary. It is suggested that

the possible actions be reviewed and developed into an action plan for strengthening the program. Appendix 3 contains a copy of the published guidelines that form the basis for the overview template. They are generally considered essential to the success of the State newborn screening system. These guidelines, entitled *U.S. Newborn Screening System Guidelines: statement of the Council of Regional Networks for Genetic Services (CORN)*, were the result of findings from multiple state consultations similar to the one conducted in Kansas. For future reference, all members of the team are available for further consultation either collectively or independently if needed.

3.0.0 Issues from the Program

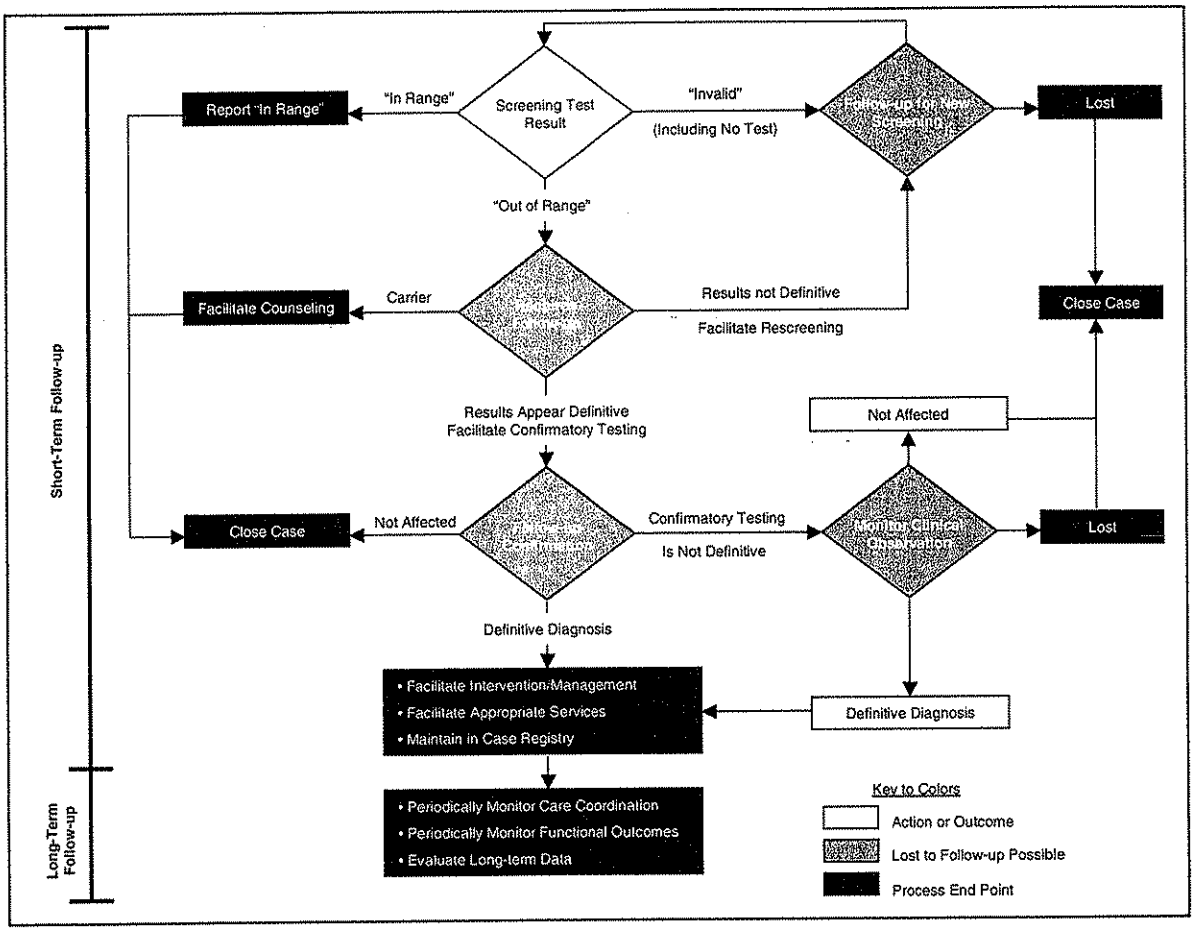
The following issues and questions were submitted to the Review Team prior to their visit and were given attention as a major focus of the review.

3.1.0 If we expand to all recommended ACMG tests, what would be the impact on the follow-up portion of the program? Staffing needs?

It is essential that there be extensive preparation and planning prior to implementation of any program expansion. Because expansion to the ACMG recommended tests would involve adding a large number of conditions to the Kansas screening panel, preparation will be extensive. To prepare adequately for the follow-up issues that will result, it is necessary that a thorough follow-up protocol be developed for each disorder to be added. The protocols should be developed in collaboration with ~~the~~ both the screening laboratory and the sub-specialty medical providers who will be providing consultation and treatment services for diagnosis and management. Examples obtained from other programs that have already implemented expanded screening should provide basic templates on which to build the Kansas protocols.

A general flow for follow-up, which should apply to all conditions included in the newborn screening panel is given below (Clinical and Laboratory Standards Institute (CLSI). *Newborn Screening Follow-up; Proposed Guideline.* CLSI document I/LA27-P, Clinical and Laboratory Standards Institute, Wayne, PA 19087). Individual follow-up protocols for each condition vary depending on the laboratory screening algorithms and the manner in which testing results are reported. For example, some results are more urgent than others and the follow-up may require more aggressive follow-up protocols. Some results may include single analytical markers and others may include multiple markers and ratios of markers. The ACMG is currently finalizing confirmatory algorithms that can serve as models on which to build a customized follow-up system that meets the needs of the Kansas program. When these models are available, they will be widely distributed and will be available on both the ACMG and NNSGRC websites.

Figure 1. General Flow Diagram for Follow-up (From CLSI I/27LA-P)



When screening newborns is required by statute, there may be explicit or implied legal exposure related to ensuring that all newborns are screened and appropriately followed. Kansas law currently requires screening for 4 conditions and it is suggested that prior to expansion, the current follow-up protocols be reviewed as a quality assurance check. Any deficiencies found should be corrected before expansion occurs. The updated protocols should provide examples to use in developing the protocols for expansion. As an example, current follow-up protocols appear to require initial notification of the newborn's physician by phone and letter, with "follow-up" to ensure compliance 30 days later. Most programs have found that a delay of 30 days to begin tracking a lost newborn often means increased tracking difficulty due to patient mobility, name changes, physician changes, etc. The sooner active follow-up begins, the higher the likelihood of finding the newborn, and the sooner medical intervention can proceed. Follow-up protocols should be reevaluated to ensure that all newborns can be located and assessed within time frames considered critical to improved health outcomes for the condition in question. Follow-up speed will become increasingly more critical as certain other conditions are added to the screening panel including CAH and MCAD deficiency among others.

Newborns whose specimens were either collected too early, were unsatisfactory

for testing all disorders or were collected after the newborn has been transfused are also at risk for not receiving a complete screen. There should be a feedback loop (see Figure 1) established so that someone, either at the laboratory or follow-up is tracking these specimens and conducting follow-up activities such as contacting the newborn's health care professional, to ensure that each of these specimens are repeated.

Screening is designed to reduce the number of newborns that might go undiagnosed by identifying those at increased risk for the disorder based on biochemical testing results. This means that some newborns will invariably be suspected to be at risk when they do not actually have the disorder in question. Depending on the screening algorithm and expected range for each screened condition, the number of patients requiring recall for further testing can be estimated. Programs implementing MS/MS screening report recall rates of 0.5-1.0% at initial start-up. The recall numbers can be reduced by vigilant follow-up and constant reevaluation of cutoff values in consultation with the medical advisors. The amount of follow-up required will not truly be known until the program is implemented and utilizing cutoff data from other programs can be critical in getting off to a good start. Of those infants recalled, the majority will have slightly out-of-range screening results that may only need repeat dried blood spot filter paper testing to ensure that levels of the biochemical marker normalize. The most frequent out-of-range findings from MS/MS testing are elevations in tyrosine concentrations due to transient tyrosinemia, multiple elevations of amino acids due to hyperalimentation, and elevations in C3 concentration.

Adding biotinidase to the screening panel could result in an increased follow-up workload depending upon the screening technology used and the goals of the screening program. That is, if the program decides to include partial biotinidase deficiency as a condition of interest, then there may be a significant increase in false positive findings during the summer due to heat denaturation of the enzyme of interest. Denaturation of normal enzyme activity in an unaffected newborn may result in an initial test interpretation of partial biotinidase deficiency. Likewise, screening protocols for CF using either an IRT/IRT protocol or an IRT/DNA protocol may result in differing amounts of follow-up.

As with all newborn screening, abnormal analytical findings reported from the newborn screening laboratory must be rapidly reported and followed up by a competent diagnostician with access to competent confirmatory laboratory services. There will always be testing results that do not clearly indicate whether or not the newborn has a medical condition requiring diagnosis and treatment. Because primary care providers are not generally familiar with the disorders that will be included in the expanded MS/MS screening panel, the program should have an expert(s) (preferably a board-certified biochemical geneticist) available for consultation and to assist with interpretation inquiries. With program expansion there should be at least two full-time follow-up personnel to manage the increased follow-up responsibilities. Consideration might also be given to these personnel sharing or assuming the responsibility for contacting providers for all cases considered to be presumptive positive cases in need of immediate follow-up.

To assist with tracking patients needing additional testing or emergency evaluation, birthing facilities, particularly the larger ones, might be asked to identify a person responsible for assisting with all newborn screening issues. In some programs, prescriptive requirements for birthing facilities of this type are included in the enabling statute or program rules. To further assist with follow-up, some programs are beginning to ask that hospital discharge coordinators make initial well-child appointments with the newborn's primary care provider prior to hospital discharge. Accurate contact information concerning the infant's medical home can save invaluable time should a test report require emergency follow-up. The identification of a medical home prior to hospital discharge is desirable and could be coordinated with other Title V programs, including the Newborn Hearing Screening Program.

In most newborn screening programs, the follow-up coordinator is also assigned the task of coordinating and/or providing program education. An early priority for expansion should be setting new educational goals and identifying strategies for their achievement. For example, the follow-up coordinator could visit the birthing centers and meet with staff members in labor/delivery/nursery areas and the laboratories on a periodic basis. In some programs, birthing facility site visits are scheduled so that all facilities are visited within a prescribed time period - perhaps 2 years. In this way, updated program information and education can be given first hand to birthing facility staff members, physicians, and laboratory professionals.

Education of health care professionals, including hospital nursery and lab staff, pediatricians, family physicians, obstetricians, midwives, prenatal education providers, is essential in order to prepare them for the program changes. KNSP should consult with the program advisory committee, medical advisors, state health professional organizations, parents, and lay advocacy groups and solicit their assistance in the educational efforts. Multi-faceted approaches may facilitate educational activities, including the use of written materials, newsletters, update announcements, and fact sheets. Presentations provided to professional groups both at professional society meetings and hospital grand rounds can help reach the target groups. Internet access to information specific to the state program can also help promote the program's goals, and assist with education.

Outreach to expectant parents and families, to ensure that they are informed about program changes, is also an important priority. Attention should be paid to keeping educational materials current and understandable for the population being served. Not only should all materials be written at an appropriate reading level, but they should also be sensitive to ethnic and cultural differences. All educational materials should have a preparation date displayed so that they may be easily determined to be current. Whenever possible, materials should be distributed at prenatal classes and prenatal medical visits so that the expectant parents will have sufficient time to learn about newborn screening and obtain additional information if needed before the birth of their baby.

Internal staff development is another program responsibility often assumed by the follow-up coordinator and the screening laboratory. Taking advantage of opportunities for staff development in the laboratory and with KDHE staff in associated programs will be

essential in adding any and all of the screening conditions considered as a part of program expansion. Likewise, it is important the appropriate staff members take advantage of outside training and professional information exchange opportunities. For example, a training course for MS/MS screening program follow-up coordinators is currently offered periodically (a cooperative effort of the NNSGRC, APHL, HRSA, and CDC). It is strongly suggested that the follow-up coordinator take advantage of this training. The course is a week-long study of the way in which MS/MS laboratory testing results should be interpreted and translated to the primary care practitioner and is limited to 8 students to increased the time available from the instructor for each student. Information exchange opportunities also exist at the national newborn screening and genetics screening symposium and at meetings of the HRSA-funded regional genetics collaboratives.

A major educational need in most programs is to decrease the number of analytically or administratively unsatisfactory specimens. In addition to a good on-site educational process at the birthing facilities, many programs have found it helpful to develop birthing facility newborn screening practice profiles. By monitoring numbers or unsatisfactory specimens, missing data elements, and other items like transport times, program quality can be dramatically improved. A Performance Evaluation and Assessment Scheme currently being developed by the NNSGRC should prove useful in identifying quality indicators. Reports of this nature can be easily established in the computerized laboratory information system, and the birthing facility monitoring and quality improvement program can be a responsibility of the follow-up coordinator.

An active educational program coupled with a comprehensive follow-up program utilizing multiple communication methods (e.g. phone, fax and letter) is more labor intensive that the current follow-up procedures. Automation of the follow-up procedures either through a computerized laboratory reporting system or through a more comprehensive departmental automated system will also impact the way in which follow-up is performed and this can also impact the number of personnel required. While much of the work of writing letters and keeping a tracking system up-to-date can be handled by a computerized system, the day-to-day operation and quality assurance require personnel. Staffing considerations will also be impacted by the number of days the laboratory is in operation. Some conditions require identification and intervention within a few days in order for screening to be useful, and therefore, testing and follow-up on a 6-day/week schedule should be considered. At a minimum, at least one more staff person to assist with education/follow-up activities will be needed. The program should also consider increasing the existing contracts with the pediatric sub-specialty care providers to cover the expected follow-up and confirmatory testing for both endocrine (CAH) and metabolic (MS/MS and biotinidase) conditions.

3.2.0 What is the estimated cost/newborn of expanding to all recommended ACMG tests?

The costs of expanding the current newborn screening program to include all of the testing recommended in the ACMG report are not easily calculated. Laboratory testing costs are dependent on the procedures chosen for the testing, the extent to which the program is computerized, whether or not testing is performed during a 5- or 6-day

workweek and various other factors. Screening laboratory costs for expansion would likely be in the $5-$10 range per patient screened. The costs associated with follow-up also vary and are directly related to the methods used in the screening laboratory, complexities of tracking protocols, days of operation, comprehensiveness of the follow-up/education process, and other factors. Follow-up/education costs generally parallel those of the laboratory so that an increase of $10 per patient would not be out of line. Costs associated with treatment are also an issue given the current statutory requirement to pay for treatment costs associated with screening. If the law remains unchanged, the costs for treatment associated with expansion could not be sustained at the current funding level. Many programs now address these funding issues by combined funding streams utilizing per-infant-screened fees (collected through billing the birthing facilities or selling the filter paper to birth facilities at the fee rate), state general funds, Federal Title V Maternal and Child Health Block grant funds, and third party reimbursement. Medicaid funding is also an issue, and is easiest handled (from the newborn screening program's point of view) through hospital negotiations apart from the screening fee.

Expansion from the currently required 4 screening test panel to the 28 (or more, depending on testing protocol) dried blood spot tests specified by the ACMG will require testing by multiple methodologies. That is, not all of the conditions on the list can be identified by MS/MS, so it will be necessary to use other testing procedures. These procedures typically identify a single primary condition in a single assay. However, with MS/MS multiple conditions can be determined simultaneously. Thus, it is possible to customize the MS/MS screening panel to include all detectable conditions or to limit the conditions detected using a decision-making process such as the one suggested by the ACMG.

Newborn screening programs that have already expanded using MS/MS have taken various approaches to implementing their MS/MS screening panels. One approach has been to mandate (add) the disorders to be screened according to a classification system that combines similar biochemical profiles [i.e. all fatty acid oxidation (FAO) disorders, all organic acid (OA) disorders, and/or all amino acid (AA) disorders]. Although many of these disorders would not individually meet traditional newborn screening prevalence criteria, when combined with all possible disorders observable with the technique, the combined prevalence is significant and meets the prevalence test. Justification for treating the disorders as a group is valid since the analytical technique, including sample preparation and analysis, is a single procedure that prepares and analyzes the sample for all of the disorders (analogous to isoelectric focusing for multiple hemoglobins). This is essentially the approach recommended in the ACMG report, although this report identified individual conditions within each category.

In addition to the approach of screening all conditions identifiable by the screening technology, a popular approach has been to mandate disorders of higher prevalence or interest as determined by screening program advisors and administrators using local screening criteria (e.g. only MCAD or only a limited group of disorders -- MCAD, MSUD, GA-I, HCY, etc.). Examples of programs that have used this approach include Wisconsin, Ohio, New Jersey, and Iowa among others. Most programs choosing this approach have collected data on the other possible screening conditions with the

intent of adding them at a later date if a significant prevalence is demonstrated. Another approach has been to mandate a limited number of disorders and offer the others as optional testing. In this approach, there is an ethical consideration to inform the parents of their rights to refuse the optional testing and to have a system of identifying the samples that should or should not be tested. Using a graded approach to adding rare metabolic disorders allows time for the program (laboratory, follow-up, and treatment) personnel to become familiar with the testing, follow-up and diagnosis process. Example of a multi-state program using this approach is Massachusetts (New England Region).

There are many questions that must be answered within the KNSP before MS/MS testing is integrated into the screening system. In the April 13, 2001 issue of the CDC publication *Morbidity and Mortality Weekly Report (MMWR)*(see Appendix 10), recommendations were provided regarding the implementation, follow-up, and diagnosis/treatment of screening disorders currently detected by MS/MS newborn screening. These recommendations resulted from a meeting held in June of 2000 in San Antonio, Texas at which an invited working group of public and private MS/MS screening programs reported their experiences. It is strongly suggested that the KNSP review the recommendations given in the MMWR as part of their considerations concerning MS/MS implementation in Kansas.

As an alternative to mandating expanded testing with MS/MS, two other options ~~that~~ have been initiated by state governments. In South Dakota, Montana, Maine and Nebraska, supplemental testing has been offered as an option, as noted in the Massachusetts model described above. The parent may or may not be responsible for the testing costs depending on program finances, and the sample is sent to a testing laboratory out of state. Summary data from the screening tests are returned to the state newborn screening program so that patients may be followed. These data have also been used in assessing the overall performance and acceptance of the program.

The second alternative is most prominent in New Jersey, where a law now requires that information about supplemental testing availability outside of the required testing program be given to parents so that they might be aware of other options. A legislative resolution suggesting a similar approach was passed in Illinois several years ago and a law similar to the New Jersey law existed in Mississippi prior to the current law that requires expanded testing. In this screening alternative, as in the one above, testing costs can be an issue, and those without the ability to pay may not be able to obtain expanded testing. This is one of the major differences between optional and mandated testing programs - in the mandated program, all newborns must receive the screening without regard to their ability to pay.

When a program decides to expand to MS/MS testing, program implementation can be a long process due to factors such as funding, instrument acquisition, operator training, pilot studies, educational activities, follow-up planning, etc. While there are ways to decrease the phase-in time, the fact remains that some lead-time is necessary before embarking on expanded MS/MS testing. Selected information from deliberations in Massachusetts are included in Appendix 7 as an example of their process for deciding on the way in which to expand their testing program. Several implementation options

exist for expanding screening services. A mandated expanded screening program will likely necessitate some sort of newborn screening fee to ensure universal coverage of all newborns. If testing is to be expanded in the KDHE laboratory, then options exist to assist with phasing in the testing capability. The most popular options for phased-in implementation are outlined below in order of acceptability to the Review Team:

1. *Prior to changing the current mandate to offer expanded screening, it may be offered as an option to parents wishing to have their newborn screened (with or without an additional charge - program option). To ensure identical testing and centralized data management, laboratory screening would be contracted to an outside laboratory (public or private) to provide the MS/MS testing in a cooperative, data-sharing partnership until services can be provided at the KDHE laboratory.*

This option allows the KNSP to maintain control over outside laboratory involvement in screening activities while working to build the infrastructure for expansion. Through a contract process, the KNSP can control the manner in which samples are collected and submitted to the testing laboratory, the way in which results are reported, and the way in which follow-up is handled. In addition to providing centralized data management, this option allows a smooth transition to the state laboratory once testing is available. Logistical difficulties that must be considered include the manner in which samples will be submitted to the testing laboratory and mechanism and amount of payment. If testing under this protocol is fee based and at the option of the parent, some will elect not to have the testing. In the contract for screening, the KNSP must clarify the amount of any testing fee and the manner in which it will be collected. If monies are to pass through the KNSP, it will likely be necessary to have a sound accounting process. A contract mechanism that leaves billing for optional testing as a responsibility of the contracting laboratory may simplify the process. The screening programs in South Dakota (using the Institute for Metabolic Disease in Dallas) and Nebraska (using Pediatrix Screening, Inc.) have experience with this option and should be contacted for further information and advice if it is considered. Other public laboratories that might be interested in a contractual arrangement to provide expanded testing include the Oregon, Iowa, Delaware and Massachusetts newborn screening laboratories.

2. *Expand the current screening mandate to include expanded testing for all of the disorders detectable by MS/MS. Contract with an outside laboratory (public or private) for MS/MS screening tests with follow-up provided by the KDHE.*

This option allows for mandatory population screening without the need to expand the KDHE laboratory to include MS/MS testing capabilities. Most of the advantages and disadvantages described in "1" above apply here with the exception that screening would be required on all newborns as part of the comprehensive newborn screening program. There would still be the need to implement a screening fee to offset expansion follow-up/administration/education

costs. Expansion to include the disorders not detected by MS/MS would require some adjustments at the KDHE, but not to the extent necessary with MS/MS. Additionally, PKU testing would be transferred to the MS/MS testing laboratory theoretically providing some space and personnel for screening tests for CAH, BIO, and CF. Should a contracted laboratory become unable to provide testing for some unforeseen reason, an alternative laboratory would be required and this eventuality should be addressed in advance.

3. *Delay requiring expanded screening until it is available at the KDHE laboratory; meanwhile, allow primary care providers (or parents) to send testing to other laboratories apart from the state program.*

The advantage of this option is that parents can immediately have access to expanded screening since it is already available in the private sector. This option suffers from the fact that parents would have to pay for the extra testing. Thus, some parents would not be able to choose to have their newborn screened because of cost issues. Additionally, information about the outcome of screening tests and the data needed to validate the value of expanded screening would not necessarily be available to the State. Duplication of some of the tests performed by the state might also occur since some private laboratories offer these tests as part of their testing panel. Experiences in other states have shown that specimen cards will occasionally be mixed up with the wrong one being sent to the state laboratory and vice versa. With this option, follow-up of screening results would typically not proceed through the public health system, but through hospitals and physicians submitting specimens. This has been found to cause a delayed diagnosis with negative consequences in at least one reported case (Eur J Pediatr 2005;164:298-301 – see Appendix 12).

3.3.0 Given Kansas' live births of just under 40,000 per year, is it more cost effective to in-source the lab work at the State Lab or to out-source? What other considerations are there in deciding whether to in-source or to out-source the Lab work?

The following paragraph from the AAP Newborn Screening Task Force Report (Pediatrics 2000;106 (suppl); p. 40. See Appendix 4 for Executive Summary) discusses some of the issues involved in considering whether to utilize a state public health laboratory for newborn screening.

> *Laboratories performing testing, in the public interest, are generally driven by 2 principal factors: cost-efficiency and quality. Ideally, newborn screening testing is inexpensive, produces high-quality results, and is technically advanced. In reality, it is often difficult to balance all of these factors within the political and economic environment of a state and a public health program. Therefore, it is incumbent on all programs to monitor laboratory performance and technological progress. It is thought that to maintain optimal quality, sufficient positive testing results should be encountered so that a positive test is easily recognized.*

There is no universally accepted standard in this regard, and high quality laboratories exist with both low and high volumes of testing. In newborn screening, it has been recommended that the threshold number of samples should be 30 000 annually.

In almost all state and territorial newborn screening systems, a public health laboratory provides testing. One potential problem is a low volume of cases and related cost and quality issues. In these cases, solutions can be sought jointly between the program and the laboratory. Some programs have found that laboratory regionalization and laboratory contracting offer possible solutions to this dilemma. Regional laboratories exist where states have agreed to pool their testing volume into a single laboratory, to maximize economies of scale. Other states use contractual arrangements with private or public laboratories. This approach may reduce costs or provide additional capacity not otherwise available. In either case, it is the responsibility of the state health agency and its newborn screening system to ensure the highest quality laboratory services for its constituents through laboratory monitoring and quality assurance procedures.

In the case of MS/MS testing, it has been found that a single MS/MS instrument can be used to analyze approximately 100,000 specimens annually. Thus, a single instrument would be somewhat underutilized in the Kansas newborns screening system. For that reason, some consideration to a regionalized MS/MS laboratory-screening center is in order. Thus, for example, it may be more efficient to submit a portion of a specimen analyzed at the KDHE laboratory for all other biochemical markers to such a regional center. At the present time, this scenario exists to some degree in Minnesota where the state public health laboratory receives all specimens, tests all but the MS/MS-specific conditions, and then forwards a portion of the specimen to the Mayo Clinic for MS/MS testing. While this approach appears to be working well within the State of Minnesota, there may be other issues when the laboratory is outside of the screening jurisdiction. Other issues that might arise in a regional testing center include: variable sample storage parameters for individual programs, variable testing panels, variations in follow-up protocols, and financing issues.

If MS/MS testing is developed in the KDHE, a start-up period of several months will be required. Other screening programs have found this period of time to cover at least 6 months. In addition to obtaining equipment, modifying computer software, developing an educational program, and developing familiarity with the conditions, there are also issues of personnel and policy that must be addressed. It may be possible to obtain the assistance of an outside laboratory as a consultant and/or service provider during the start-up period. An arrangement of this type would help to ensure that the Kansas program did not encounter the same start-up deficiencies as already seen by other programs. It is not necessary to commit mistakes in start-up for which solutions have already been implemented.

3.4.0 Does Kansas have the necessary state infrastructure to expand its state newborn screening program?

The newborn screening system is more comprehensive than just the screening laboratory, and all aspects of the system infrastructure (testing, follow-up, diagnosis, management, evaluation, and education) must be considered. There is a basic system infrastructure already in place that encompasses laboratory testing, follow-up, education and clinical services. Expansion of the program would include additional testing for endocrine and metabolic conditions along with CF. All increases in screening would likely require additional equipment and personnel in the laboratory, additional follow-up for increases in presumptive cases for the various conditions, and increased confirmatory activities on the part of the clinician. While the endocrine and metabolic conditions represent increased infrastructure needs, screening for CF will require additional infrastructure considerations, particularly as it relates to referrals for sweat testing and diagnosis. Thus, for CF screening additional considerations must be made that include interactions and partnerships with the cystic fibrosis centers. Such partnerships are not currently in place. These considerations can be simplified by contacting a state program that has already experienced adding CF screening to a program of similar size and resources.

Expansion to include MS/MS testing presents unique challenges because of the sophistication and relative complexity of the equipment that must be mastered for quality screening. Experiences in other state public health laboratories are outlined in the workgroup recommendations below from the April 13, 2001 *MMWR Recommendations and Report*:

- *Operators of MS/MS instruments should hold a minimum of a Bachelor of Science degree in a laboratory science or medical technology. In addition, they must meet the pertinent Clinical Laboratory Improvement Amendments of 1988 personnel requirements. Additionally, MS/MS laboratorians should have: a) mechanical aptitude, b) computer skills, and c) an interest in mass spectrometry technology. Each instrument requires one primary laboratorian and a backup. Laboratories having multiple instruments should have an equal number of personnel plus one or two laboratorians, depending on whether the supervisor serves as the backup.*

- *Managers and supervisors of MS/MS operations should have background experience in mass spectrometry. One manager is sufficient to oversee multiple instruments.*

- *Newborn screening laboratories should develop a backup plan for instrument downtime. That plan should include ready access to additional instruments or backup laboratories.*

Operational newborn screening laboratories with MS/MS experience have performed extensive testing to establish abnormal acylcarnitine and amino acid profiles for the disorders they are reporting. Preliminary data shared between programs seems to show good analytical agreement in spite of different instrumentation in use. Sharing cutoff information between laboratories should help minimize the start-up period for new MS/MS programs such as under consideration in Kansas. Due to the possible unfamiliarity of primary care providers with conditions detected by MS/MS, the program should have an expert(s) (preferably a board-certified biochemical geneticist) available to assist with interpretation inquiries. Inquiries by the Review Team seemed to indicate that sufficient biochemical expertise is available in Kansas or alternatively in nearby Missouri.

As with all newborn screening, abnormal analytical findings reported from the newborn screening laboratory must be followed up by a knowledgeable diagnostician with access to competent confirmatory laboratory services. There will always be testing results that do not clearly indicate whether or not the newborn has a medical condition requiring diagnosis and treatment. Screening is designed to reduce the number of patients that might go undiagnosed by identifying those at risk for the disorder. This means that some will be identified that do not have the disorder suspected. The idea of improving screening techniques through program evaluation is to reduce these 'false positive' findings while eliminating the 'false negatives.' The amount of follow-up required will not truly be known until the program is implemented, but data from other programs should be helpful in making these determinations for planning purposes. It is suggested that reports from other states be closely analyzed in this regard. As noted previously, most programs appear to be experiencing initial recall of 0.5-1.0% with MS/MS, which diminishes with time and experience. The recall rate with CAH is approximately the same as with CH or about 0.5%. Comparatively the amount of recall for other conditions will be considerably lower.

Given the cost experiences in other programs relative to the testing, follow-up and support system necessary for expansion, it is the opinion of the Review Team that the current finances would have to be significantly increased to appropriately support a full-service expanded program. Because of current budgetary constraints within the State budgeting system, expansion would likely require some fee support. In order to adequately prepare for expansion, a detailed proposal should be prepared in consultation with stakeholders in the newborn screening system (i.e. the advisory committee and the KDHE). Since screening for CF is included in the ACMG recommended panel, representation from the CF community, including health professionals, patients and families should also be involved. The expansion proposal should detail anticipated costs for laboratory equipment, expendable supplies, laboratory and follow-up/education personnel, educational activities, follow-up activities and any associated diagnostic and treatment costs deemed suitable for inclusion by the advisory group. Included in discussion should be representatives of the hospital association, third-party payers, Medicaid, and CSHCN. Once the appropriate system to meet anticipated needs has been defined, a thorough cost analysis should be completed and elements of a fee system considered. Fee implementation can be a complex undertaking and as such, its details should be carefully considered and planned.

In the interim, prior to expansion, steps should be taken to share information with the public about alternatives available to supplement the universal newborn screening requirements currently in effect.

3.5.0 Are there any states with expanded NBS programs that are doing so through regional or state partnerships? What are Kansas' best options if we were to utilize such partnerships?

There are several partnership models available. Almost since screening began, there have been partnerships in the Northwest and the Northeast where small numbers of births contributed to regionalization for improved cost effectiveness and program quality and efficiency. Thus the states of Oregon, Nevada, Idaho, Hawaii and Alaska partner to utilize the screening laboratory in Oregon. In this scenario, all states in the region are required to obtain identical laboratory screening analyses and interpretations by the Oregon laboratory. This is in contrast to the Northeast regional program where the states of Massachusetts, Maine, New Hampshire, Vermont, Connecticut and Rhode Island obtain customized screening laboratory services from the University of Massachusetts screening laboratory.

Public-public screening partnerships also exist between North Dakota and Iowa, and between Colorado and certain out-of-state military and Indian Health Services birthing facilities. Three programs, D.C, Nebraska and Mississippi partner with Pediatrix Screening, Inc. to obtain their laboratory testing and in two of them (NE and MS), a significant portion of the screening fee is returned to the state health department to pay for related follow-up and education. The South Dakota program currently partners with a private in-state laboratory for routine tests, the Massachusetts screening laboratory for CF testing, and the Institute for Metabolic Diseases (Dallas, TX) for MS/MS testing. The Montana program utilizes the services of the Wisconsin public health laboratory for optional MS/MS testing. Programs in Louisiana, Maryland and Pennsylvania allow Pediatrix Screening, Inc. to provide testing for some hospitals and the Pennsylvania program also contracts with Pediatrix Screening, Inc. and the University of Massachusetts screening laboratory for state required testing. California has a unique arrangement in which 8 commercial laboratories are provided contracts to utilize equipment owned by the state program to conduct testing according to state specifications. The state public health laboratory provides close oversight. In a similar contractual arrangement, follow-up services in California are also decentralized into regional contracts.

There are multiple options available to the Kansas program. In any considerations that would not utilize the current screening laboratory, consideration must be given to the possibility that any contractual arrangement might end suddenly for unforeseen problems. If that occurs with the KDHE laboratory no longer operational, it would be unlikely that the KDHE laboratory could be reconstituted to perform screening tests because of the massive expense and logistics that would have to be overcome. For this reason, the Review Team would suggest that any expansion considerations include utilization of the state screening laboratory in some way, either as the primary screening test provider or as one of the screening test providers. Likewise, if outsourcing of any part of the program is a consideration, then care must be taken to ensure that the arrangement would allow the

state program to meet its public health responsibilities. Items such as timely transport of specimens, ownership of the NBS specimens and any generated data should be clearly specified and defined, and evaluation data remain centralized with ready accessibility to state public health policy makers. If alternative testing strategies are considered, then it would be best to initiate a dialogue with one of the programs previously named who is utilizing the model preferred. Any decisions concerning program structure and functions should involve the appropriate stakeholders and should be developed for the ultimate benefit of Kansas citizens. The Review Team does not consider itself qualified to recommend a "best" model for Kansas.

3.6.0 Is there a formula for determining treatment costs associated with expansion?

A formula for determining treatment costs associated with newborn screening expansion does not exist. Alternatively, it is informative to look at some of the reported studies on cost effectiveness of screening. Several examples are given below with pertinent summary statements in an effort to provide some information as to treatment and cost effectiveness of expansion.

Reference: Venditti LN, Venditti CP, Berry GT, Kaplan PB, Kaye EM, Glick H, Stanley CA. *Newborn screening by tandem mass spectrometry for medium-chain acyl-CoA dehydrogenase deficiency: a cost-effectiveness analysis.* Pediatrics 2003;112:1005-15.

> *The clinical course of infants who have true positive screens for MCADD is also not fully understood. We used primary data, derived from retrospective chart review, to construct a database similar to that for the unscreened patients with MCADD and derived estimates of event probabilities and cost estimates for the first 10 years of patients' lives. Expert opinion was used to estimate resource use beyond the 10th year of life.*
>
> *On the basis of these data, we assumed that all children who test positive for MCADD have their diagnoses confirmed during an initial outpatient specialty visit. The workup during this visit was assumed to include a repeat acylcarnitine profile, carnitine quantitation, urine organic acid analysis, and mutation studies if they had not been performed before the visit. We assumed that all newborn screen-positive patient-families would receive extensive education and emergency department protocols, special diets would not be prescribed, supplemental carnitine would not be administered in the well state, and parents would not be instructed to use glucometers. We examined all of these parameters in sensitivity analyses. Finally, we assumed that MCADD-positive patients would utilize the emergency department for intravenous glucose during times of intercurrent illness with clinical event probabilities similar to our cohort but otherwise were well and experienced no episodes or sequelae of severe metabolic decompensation.*

Conclusion:

In our base-case analysis over the first 20 years of life, the cost of newborn screening for MCADD was approximately $11 000 (2001 US dollars; 95% CI: <$0–$33 800) per life-year saved, or $5600 (95% CI: <$0–$17 100) per quality-adjusted life-year saved compared with not screening. Over a 70-year horizon, the respective ratios were approximately $300 (95% CI: <$0–$13 000) and $100 (95% CI: <$0–$6900). The results were robust when tested over plausible ranges for diagnostic test sensitivity and specificity, MCADD prevalence, asymptomatic rate, and screening cost.

Schoen EJH, Baker JC, Colby CJ, To TT. *Cost-benefit analysis of universal tandem mass spectrometry for newborn screening.* Pediatrics 2002;110:781-6.

Internal cost data were obtained from the Kaiser Permanente (KP) Cost Management Information System, an automated system, which integrates KP's Northern California Regional Medical Utilization database and the KP General Accounting Ledger and itemizes fully allocated costs by department, by medical center, by patient, and by procedure. Cost Management Information System also uses data from a separate referral database of medical utilization at non-KP facilities.

In addition, cost estimates for treatment and follow-up were based on information from the KP Regional Metabolic Clinic, which currently manages metabolic disorders in over 200 children, including 7 children with maple syrup urine disease (MSUD), with methylmalonic acidemia (MMA) or propionic acidemia (PPA), and 96 with PKU. In addition to these internal data, our analysis included amounts of required follow-up care estimated by our 4 metabolic geneticists on the basis of their experience.

Conclusion:

Because severe clinical manifestations of many whether detected presymptomatically (ie, by screening) or after symptoms manifest, IEM in infants and children is expensive to manage. Our finding that the cost of MS/MS screening per quality adjusted year of life compares favorably with costs of other accepted screening procedures and supports a policy of encouraging MS/MS screening. However, when a program of NBS using MS/MS is financed, the calculations should consider total expenses, including costs not only of equipment and analysis but also costs of training, personnel, tracking test results, counseling parents, supplying special diets and specialty care, and clinical follow-up.

3.7.0 Are there enough data/experience from states with expanded NBS and united availability of genetics programs or other specialists to show access is a real or theoretic issue if expanded screening identifies more children with metabolic errors?

Experiences with expanded MS/MS screening to date indicate that the amount of recall resulting in the need for access to clinical subspecialty services is generally considered manageable within the available resources. Hard data have not been published in this regard, but projects are underway to ascertain the extent of genetic services utilized as a result of newborn screening and the available services. It is hoped that project results will provide some answers to questions about accessibility and availability of genetic services. As indicated previously, the amount of recall experienced by MS/MS expansion varies between 0.5-1.0% depending on whether the program is experienced or not. These numbers are approximately the same as the recall experienced with CH and with CAH, particularly when screening for them initially began. In order to partially address the concerns in some jurisdictions that subspecialty services would be inadequate, HRSA has funded regional genetics collaboratives to assess this issue and to optimize regional resources for improved access to genetic services. The KNSP is encouraged to become involved in the Region 5 regional activities surrounding newborn screening services as a way of maximizing service availability.

3.8.0 What change would Kansas see in annual number of SIDS deaths if we were to expand NBS to all ACMG recommended tests? (2003 -- 33 SIDS deaths in KS)

A study to determine whether metabolic conditions detectable by MS/MS might be a contributor to deaths from Sudden Infant Death Syndrome (SIDS) was conducted between 1996 and 2001. Some comments about this study published in the July 25, 2003 MMWR are given below in answer to this question. Based on the data presented below, approximately one SIDS death would be ruled out every three years in Kansas if expanded screening was mandated for all newborns. Further references include:

Boles R, Buck E, Blitzer M. *Retrospective biochemical screening of fatty acid oxidation disorders in postmortem livers of 418 cases of sudden death in the first year of life.* J Pediatr 1998;132:924–33.

Chace D, DiPerna J, Mitchell B, Sgroi, B, Hofman L, Naylor E. *Electrospray tandem mass spectrometry for analysis of acylcarnitines in dried postmortem blood specimens collected at autopsy from infants with unexplained cause of death.* Clin Chem 2001;47:1166–82.

Wilcox R, Nelson C, Stenzel P, Steiner R. *Postmortem screening for fatty acid oxidation disorders by analysis of Guthrie cards with tandem mass spectrometry in sudden unexpected death in infancy.* J Pediatr 2002;141:833–6.

Excerpts from MMWR for July 25, 2003:

> *Sudden infant death syndrome (SIDS), or the death of an infant aged <1 year that remains unexplained after a thorough investigation, is*

the third most common cause of death among infants in the United States. Sudden, unexplained deaths also occur among children aged >1 year; however, the number of these deaths is not well documented. Certain cases of SIDS and sudden unexplained death beyond infancy might be attributable to complications of unrecognized metabolic diseases. Tandem mass spectrometry (tandem MS) can be used to screen for several of these disorders. Despite the low prevalence of these diseases, newborn screening for these disorders has been found to compare favorably with the cost of other screening programs. However, the contribution of these diseases to early childhood deaths is not well understood. To determine the proportion of sudden, unexpected early childhood deaths associated with selected metabolic diseases, CDC, the Office of the Chief Medical Examiner in Virginia, and a private laboratory conducted a population-based study. This report summarizes the results of the study, which indicate that 1% of children had a positive postmortem metabolic screen using tandem MS. Of the eight children with positive screening tests, seven might have had improved outcomes had they been identified and treated during the newborn period. The use of tandem MS in newborn screening programs could offer an opportunity to prevent early childhood mortality.

Editorial Note:

The findings in this report suggest that, during 1996–2001, undiagnosed metabolic diseases were contributing factors in 1% of unexpected deaths in young children in Virginia. Postmortem metabolic screening might have identified a cause of death for certain children who died unexpectedly. Because three of the children with positive tandem MS metabolic screens did not have fat in their livers, performing postmortem metabolic disease screening on the basis of abnormal liver pathology might not have identified all affected children. Approximately 5% of sudden infant deaths might be associated with metabolic diseases. The postmortem identification of affected children should prompt testing of siblings who might be affected by the same genetic disorder and might benefit from effective interventions. No population-based studies of survival have been performed for these conditions. Of the eight children with positive tandem MS metabolic screening tests, seven might have had improved outcomes if they had been identified by newborn screening and effective therapy had been initiated in time to prevent their deaths. Newborn screening programs considering including testing for metabolic diseases that can be detected by tandem MS can use these results to estimate the number of children who might benefit from early identification and treatment.

The findings in this report are subject to at least three limitations. First, no test was available to confirm that six of the identified children had the disease suggested by tandem MS metabolic screening. However, the predictive value of tandem MS metabolic screening using postmortem blood is high for the fatty acid oxidation disorders identified. The positive

predictive value of tandem MS metabolic screening for organic acidemias has not been established. Second, the contribution of metabolic diseases that can be identified by tandem MS to unexpected deaths might be underestimated. Affected persons sometimes die after age 3 years, and these persons were excluded from this study. In addition, children included in this study died in a manner that caused their deaths to fall under the jurisdiction of the Virginia ME; other deaths were not studied. All previously healthy children in Virginia who died suddenly or of an unknown cause should have been referred to the ME and would have been eligible for the study; however, a child with an undiagnosed metabolic disease who was under the care of a physician and whose death was attributed to another apparently clear cause (e.g., infection) might not have been referred. Finally, the sensitivity and specificity of tandem MS using postmortem blood is not known.

The data in this report illustrate one aspect of the natural history of the diseases detectable by tandem MS and could be useful to programs considering the addition of this technology to their newborn screening programs. These programs should consider several factors when deciding to add tests for metabolic diseases, including the prevalence and natural history of the diseases, the availability of effective interventions, the costs and benefits of newborn screening, and the reliability of available screening technologies.

3.9.0 How many states have not expanded their newborn screening programs?

Information about testing in the various states is kept updated On Line at http://genes-r-us.uthscsa.edu. The report as of January 10, 2006 follows:

National Newborn Screening and Genetics Resource Center
Austin, Texas USA
NNSGRC

National Newborn Screening Status Report

U.S. National Screening Status Report

Updated 01/10/06

The U.S. National Screening Status Report lists the status of newborn screening in the United States.

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D = likely to be detected (and reported) as a by-product of MRM screening (MS/MS) targeted by Law or Rule

STATE	Core[1] Conditions									Additional Conditions Included in Screening Panel (universally required unless otherwise indicated)
	Hearing	Endocrine		Hemoglobin			Other			
	HEAR	CH	CAH	Hb S/S	Hb S/A	Hb S/C	BIO	GALT	CF	
Alabama	A	●	●	●	●	●	●	●		
Alaska	A	●	●	●	●	●	●	●		
Arizona	A	●	●	●	●	●	●	●		
Arkansas	●	●		●	●	●		●		
California	B	●	●	●	●	●		●		5-OXO; HHH; PRO
Colorado	●	●	●	●	●	●	●	●	●	
Connecticut	●	●	●	●	●	●	●	●	B	5-OXO; HHH; HIV[2]; NKH
D.C.	●	●		●	●	●		●		G6PD
Delaware	A	●	●	●	●	●		●		
Florida	●	●	●	●	●	●	●	●	C	
Georgia	A	●	●	●	●	●	●	●		
Hawaii	●	●	●	●	●	●	●	●		
Idaho	A	●	●	●	●	●	●	●		
Illinois	●	●	●	●	●	●	●	●		5-OXO
Indiana	●	●	●	●	●	●	●	●		
Iowa	●	●	●	●	●	●	●	●	●	HHH; NKH
Kansas	●	●		●	●	●		●		
Kentucky	A	●	C	●	●	●	C	●	C	
Louisiana	●	●		●	●	●	●	●		
Maine	A	●	●	●	●	●	●	●		HHH (A); CPS (D)
Maryland	●	●	●	●	●	●	●	●	C	
Massachusetts	●	●	●	●	●	●	●	●	A	TOXO; HHH (A); CPS (D)
Michigan	A	●	●	●	●	●	●	●		
Minnesota	A	●	●	●	●	●	●	●	C	
Mississippi	●	●	●	●	●	●	●	●	●	5-OXO; CPS; HHH
Missouri	●	●	●	●	●	●	C	●	C	
Montana	●	●	B	●	●	●	B	●	B	
Nebraska	A	●	●	●	●	●	●	●	●	5-OXO; HHH; NKH (A)
Nevada	A	●	●	●	●	●	●	●		
New Hampshire	A	●	C	C	C	C	C	●	C	TOXO
New Jersey	●	●	●	●	●	●	●	●	●	
New Mexico	●	●	●	●	●	●	●	●	C	
New York	●	●	●	●	●	●	●	●	●	HIV
North Carolina	●	●	●	●	●	●	●	●		
North Dakota	A	●	●	●	●	●	●	●	●	
Ohio	●	●	●	●	●	●	●	●		
Oklahoma	●	●	●	●	●	●		●	●	
Oregon	A	●	●	●	●	●	●	●		
Pennsylvania	●	●	●	●	●	●	B	●	B	5-OXO; CPS; G6PD; HHH; NKH (B)
Rhode Island	●	●	●	●	●	●	●	●		
South Carolina	A	●	●	●	●	●	●	●	●	
South Dakota	A	●	●	●	●	●	●	●	B	5-OXO; EMA; HHH; NKH
Tennessee	A	●	●	●	●	●	●	●		5-OXO; HHH; NKH
Texas	A	●	●	●	●	●		●		
Utah	●	●		●	●	●		●		
Vermont	A	●	●	●	●	●	●	●		CPS
Virginia	●	●	●	●	●	●	●	●	C	
Washington	A	●	●	●	●	●	●	●		
West Virginia	●	●		●	●	●		●		
Wisconsin	A	●	●	●	●	●	●	●	●	
Wyoming	●	●	●	●	●	●	●	●	●	

[1]Terminology consistent with ACMG report - Newborn Screening: Toward a Uniform Screening Panel and System 2005. p. 63.

[2]Newborn screened for HIV only if mother was not screened during pregnancy

Deficiency/Disorder Abbreviations and Names

BIO	Biotinidase	**CF**	Cystic fibrosis	**GALT**	Transferase deficient galactosemia (Classical)	**HB S/C**	Sickle – C disease	**HEAR**	Hearing screening
CAH	Congenital adrenal hyperplasia	**CH**	Congenital hypothyroidism	**HB S/S**	Sickle cell disease	**HB S/A**	S-βeta thalassemia		

Other Disorders

5-OXO	5-oxoprolinuria (pyroglutamic aciduria)	**G6PD**	Glucose 6 phosphate dehydrogenase	**NKH**	Nonketotic hyperglycinemia
CPS	Carbamoylphosphate synthetase	**HHH**	Hyperammonemia/ornithinemia/ citrullinemia (Ornithine transporter defect)	**PRO**	Prolinemia
EMA	Ethylmalonic encephalopathy	**HIV**	Human immunodeficiency virus	**TOXO**	Toxoplasmosis

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STATE	Core[1] Conditions - Metabolic																			
	Fatty Acid Disorders					Organic Acid Disorders									Amino Acid Disorders					
	CUD	LCHAD	MCAD	TFP	VLCAD	GA-1	HMG	IVA	3-MCC	CBL-A,B	BKT	MUT	PROP	MCD	ASA	CIT	HCY	MSUD	PKU	TYR-1
Alabama	●		●							●		●	●			●	●	●	●	●
Alaska	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Arizona																	●	●	●	
Arkansas																			●	
California	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Colorado	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	●	C
Connecticut	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
D. of Columbia																	●	●	●	
Delaware		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Florida	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Georgia			●														●	●	●	●
Hawaii	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Idaho	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Illinois		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Indiana	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Iowa	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Kansas																			●	
Kentucky	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	●	C
Louisiana			A												A	A	A	A	●	
Maine	D	●	●	D	●	●	●	●	●	●	●	●	●	D	●	●	●	●	●	●
Maryland		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Massachusetts	D	A	●	D	A	A	A	A	A	A	A	A	A	D	A	A	●	●	●	A
Michigan	A	A	●	A	A	A	A	A	A	A	A	A	A	A	●	●	●	●	●	A
Minnesota	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Mississippi	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Missouri		●	●	●	●	●	●	●	●	●			●		●	●	●	●	●	
Montana	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	●	B
Nebraska		A	●	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	●	A
Nevada	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
New Hampshire			C														●	●	●	
New Jersey		A	●	A	●	●	●	●	●	●	A	●	●		●	●	A	●	●	A
New Mexico	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	●	C
New York	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
North Carolina		●	●	●	●	●	●	●	●	●	●	●	●		●	●	●	●	●	
North Dakota		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Ohio		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
Oklahoma			C																●	
Oregon	A	●	●	A	●	●	●	●	●	A	A	●	●	A	●	●	●	●	●	●
Pennsylvania	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	●	●	B
Rhode Island	D		●														●	●	●	
South Carolina	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
South Dakota	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Tennessee		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Texas																			●	
Utah	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Vermont	D	●	●	D	●	●	●	●	●	●	●	●	●	D	●	●	●	●	●	●
Virginia	C	C	●	C	C	C	C	C	C	C	C	C	C	C	C	C	●	●	●	C
Washington			●														●	●	●	
West Virginia																			●	
Wisconsin	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Wyoming																			●	

[1]Terminology consistent with ACMG report - Newborn Screening: Toward a Uniform Screening Panel and System 2005. p. 63.

Deficiency/Disorder Abbreviations and Names (optional nomenclature)

3-MCC	3-Methylcrotonyl-CoA carboxylase	CUD	Carnitine uptake defect (Carnitine transport defect)	LCHAD	Long-chain L-3- hydroxyacyl-CoA dehydrogenase	PKU	Phenylketonuria/ hyperphenylalaninemia
ASA	Argininosuccinate acidemia	GA-1	Glutaric acidemia type 1	MCAD	Medium-chain acyl-CoA dehydrogenase	PROP	Propionic acidemia (Propionyl-CoA carboxylase)
BKT	Beta ketothiolase (mitochondrial acetoacetyl-CoA thiolase ; short-chain ketoacyl thiolase: T2)	HCY	Homocystinuria (cystathionine beta synthase)	MCD	Multiple carboxylase (Holocarboxylase synthetase)	TFP	Trifunctional protein deficiency
CBL A,B	Methylmalonic acidemia (Vitamin B12 Disorders)	HMG	3-Hydroxy 3 - methylglutaric aciduria (3-Hydroxy 3-methylglutaryl-CoA lyase)	MSUD	Maple syrup urine disease (branched-chain ketoacid dehydrogenase)	TYR-1	Tyrosinemia Type 1
CIT I	Citrullinemia type I (Argininosuccinate synthetase)	IVA	Isovaleric acidemia (Isovaleryl-CoA dehydrogenase)	MUT	Methylmalonic Acidemia (methylmalonyl-CoA mutase)	VLCAD	Very long-chain acyl-CoA dehydrogenase

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STATE	Secondary Target[1] Conditions																									
	Fatty Acid Disorders								Organic Acid Disorders						Amino Acid Disorders								Other Metabolic		Hbg
	CACT	CPT-Ia	CPT-II	DE-RED.	GA-II	MCKAT	MSCHAD	SCAD	2M3HBA	2MBG	3MGA	CblC,D	IBG	MAL	ARG	BIOPT-BS	BIOPT-RG	CIT-II	H-PHE	MET	TYR-II	TYR-III	GALE	GALK	Variant hemoglobins
Alabama												●						●	●		●	●			A
Alaska	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●		B	B	●
Arizona																			●						A
Arkansas																			●				●	●	A
California	●	●	●		●			●	●	●	●	●	●	●	●	A	A	●	●	●	●	●			●
Colorado	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C			C	●	C	C	C			●
Connecticut	●	●	●	●	●			●				●		●	●				●	●			●	●	A
D. of Columbia																			●				●	●	A
Delaware	●		●		●	A		●	A	●	A	●	●		●	A	A	●	●	●	●	●	●	●	●
Florida	●	●	●		●			●				●						●	●	●	●				A
Georgia																B	B		●				●	●	●
Hawaii	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●		B	B	A
Idaho	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●		B	B	●
Illinois	●	●	●		●		●	●		●	●	●	●	●	●			●	●	●	●	●	●	●	A
Indiana	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●				A
Iowa	●	●	●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●				A
Kansas																			●						A
Kentucky								C											●						A
Louisiana																			●						A
Maine	D	D	●		●			●		D	D	●	D		●			●	●	D	●	D	●	●	●
Maryland	●		●		●		●	●		●	●	●	●		●	B	B	●	●	●	●	●	●	●	A
Massachusetts	D	D	A		A			A		D	D	A	D		A			A	●	D	A	D	●	●	●
Michigan	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A			●	●						A
Minnesota	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Mississippi	●	●	●	A	●	A	●	●	A	●	●	●	●	●	●	A	A	●	●	●	●	A	●	●	●
Missouri	●	●	●		●			●				●						●	●	●	●	●			●
Montana	B		B	B	B	B	B	B		B	B	B	B	B		B	B	B	●	B	B	B			●
Nebraska	A		A		A			A		A		A	A	A	A			A	●	A	A		●	●	A
Nevada	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●		B	B	A
New Hampshire																			●	D			●	●	B
New Jersey	A		A		A		A	●		A	A	●	A	A		●	●	●	●	A	A	A			A
New Mexico																			●						A
New York	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●	●	●	●	●			●
North Carolina					●			●		●		●	●						●	●	●	●			A
North Dakota	●	●	●		●	●	●	●	●	●	●	●	●	●	●				●		●				A
Ohio	●	●	●		●			●		●		●	●		●			●	●	●					A
Oklahoma																			●						A
Oregon	●	A	●		●			●	A	A	●	●	A	A	A	B	B	●	●	●	●		B	B	●
Pennsylvania	B	B	B	B	B		B	B		B	B	B	B	B	B	B	B	B	●	B	B	B	●	●	A
Rhode Island		D																	●				●	●	●
South Carolina	●		●		●	●		●	●	●	●	●	●			●	●	●	●	●			●	●	A
South Dakota	●	●	●		●			●		●	●	●	●	●	●			●	●	●	●	●			●
Tennessee	●	●	●	●	●			●	●	●	●	●	●	●	●			●	●	●	●	●			●
Texas																			●						A
Utah	●	●	●		●			●	●	●		●	●		●	●	●	●	●	●	●	●			●
Vermont	D	D	D		D					D	D	●			D			●	●	D	D	D	●	●	●
Virginia																			●						A
Washington																			●						A
West Virginia																			●				●	●	A
Wisconsin	●		●	●	●	●	●	●		●	●	●	●	●		●	●	●	●	●	●	●			●
Wyoming																			●						●

[1]Terminology consistent with ACMG report - Newborn Screening: Toward a Uniform Screening Panel and System 2005, p. 63.

Deficiency/Disorder Abbreviations and Names (optional nomenclature)

2M3HBA	2-Methyl-3-hydroxy butyric aciduria	CACT	Carnitine acylcarnitine translocase	GA-II	Glutaric acidemia Type II	MAL	Malonic acidemia (Malonyl-CoA decarboxylase)
2MBG	2-Methylbutyryl-CoA dehydrogenase	CBL-C,D	Methylmalonic acidemia (Cbl C,D)	GALE	Galactose epimerase	MCKAT	Medium-chain ketoacyl-CoA thiolase
3MGA	3-Methylglutaconic aciduria	CIT-II	Citrullinemia type II	GALK	Galactokinase	MET	Hypermethioninemia
ARG	Argininemia (Arginase deficiency)	CPT-Ia	Carnitine palmitoyltransferase I	H-PHE	Benign hyperphenylalaninemia	SCAD	Short-chain acyl-CoA dehydrogenase
BIOPT-BS	Defects of biopterin cofactor biosynthesis	CPT-II	Carnitine palmitoyltransferase II	IBG	Isobutyryl-CoA dehydrogenase	TYR-II	Tyrosinemia type II
BIOPT-REG	Defects of biopterin cofactor regeneration	De-Red	Dienoyl-CoA reductase	M/SCHAD	Medium/Short chain L-3-hydroxy acyl-CoA dehydrogenase	TYR-III	Tyrosinemia type III

3.10.0 If we expanded our newborn screening tests, what increase would we expect in numbers of presumptive positive results?

The issue of recall for the various conditions that might be added has been addressed in some of the previous comments. Programs typically experience higher recall numbers when they are just beginning a new procedure. This is partly due to the tendency of new programs to be conservative in their approach so as not to miss cases and partly due to inexperience. In cases where use of a commercial kit is involved, increased numbers of newborns recalled may result from the use of manufacturer's cutoff values, which may be set conservatively so that cases of the condition in question are not missed. As data are accumulated, these cutoff values can be adjusted. Similarly, case detection data can be used to modify the conservative approach of start-up programs.

Experience among Review Team members indicates that the amount of recall for CAH will likely be around 0.5% of the total screened, similar to CH. For BIO, the amount of recall will depend upon whether or not the testing goals include detection of "partial" as well as "classical" cases of biotinidase deficiency. If the goal is to detect only classical cases, then there should be very few (1-2) positives per year. If the goal is to include detection of "partial" biotinidase deficiency then the recall will be higher, possibly as high as 0.1% of the total screened depending on the cutoff used. For CF, regardless of the methodology and cutoff (# of mutations screened) a recall of 0.2-0.3 percent can be expected.

3.11.0 Do states with expanded screening get complaints from parents and other consumers? Costs to parents?

The Review Team is unaware of any program that has received complaints from parents and other consumers for expanding their newborn screening programs. On the contrary, there are several lay advocacy groups that have openly criticized programs that have not expanded their screening programs. Numerous articles have appeared in lay publications and local newspapers supporting the concept of expanded screening. While for-profit laboratories may charge between $25-75 for expanded newborn screening, there are many advocacy groups supporting expansion. In Mississippi, New Jersey, and Illinois (and possibly others), parents were responsible for legislative actions that resulted in requirements to inform parents of screening services available outside of the state required screening program.

It is important to include the concept of public health in any newborn screening considerations. Newborn screening is a multi-part system that includes many different persons and groups to keep it functioning effectively. In cases where parents opt to have their newborn screened outside of the KNSP, it is important that a fully functional screening system be in place. Follow-up of the testing results usually require additional testing and/or subspecialty involvement when an out-of-range result is encountered. While the public health system that supports the newborn screening program includes all of the steps necessary in screening, detection, and patient management, a private laboratory system may not. This has been found to cause a delayed diagnosis with negative consequences in at least one reported case (Eur J Pediatr 2005;164:298-301 –

see Appendix 11).

3.12.0 What is the general hospital reaction to expanded screening in the states?

The hospital functions within the newborn screening system to provide part of the education to parents, the screening specimen collection and submission, record keeping, and assistance with patient tracking. In a fee-based newborn screening system, the hospital is often responsible for the cost of screening and ultimately must recover these costs through third-party payers, including Medicaid. Because of the complexities of the payment and reimbursement process, it is usual for hospitals to react somewhat adversely to expanded screening because it usually means an increased expense that may not be compensated.

Currently, the most popular method for collecting fee revenue across the country is through the sale of newborn screening collection kits. Some programs bill monthly for testing services based on records of specimens tested at the screening laboratory. Other programs bill on the basis of birthing records submitted from hospitals to the screening program showing the numbers of specimens submitted over a specified time interval. In all of these cases, the cost of screening is ultimately a hospital charge and is generally included in the global birthing fee/reimbursement that exists for maternity services.

While costs are not currently a significant concern to hospitals within Kansas due to the current newborn screening financing mechanism, implementation of a fee-based screening system to pay for all or part of expansion will likely result in financial impact and concern to the hospitals. It will be important to include representation from hospitals in deliberations that may result in fees that impact them. Likewise, because there will also likely be an impact on third-party payers and Medicaid, these groups should also be engaged and included in the deliberations. Experiences from programs have varied concerning reactions of hospitals to increased testing (and cost), and these reactions have often been the result of whether or not they were included in the financing discussions. Any discussions and deliberations should focus on the positives and emphasize improvement in quality of care for the newborn/infant population.

3.13.0 What is the role of Medicaid in most states?

Medicaid funding plays an important role in most states. Approximately one-third of the births nationally qualify for Medicaid services. Since most programs charge a fee for newborn screening, the fee payer is usually the party responsible for obtaining Medicaid reimbursement. The two primary fee mechanisms include sale of newborn screening kits and direct billing to the specimen submitter. Since hospitals are the major payers in these scenarios, it is important to consider their means of Medicaid reimbursement when considering newborn screening finances. The usual method for Medicaid reimbursement to hospitals is through their negotiated maternity fees. A limited number of programs obtain Medicaid support through direct reimbursement. The excerpts below from the 2003 Report to Congressional Requestors from the Government Accounting Office (*Newborn Screening Programs: Characteristics of State Programs*,

March 2003, pp. 16-17) summarize the extent of Medicaid involvement in screening program finances.

> *Fees are the largest funding source for most states' newborn screening programs. Forty-three states reported they charge a newborn screening fee to support all or part of program expenditures. The fees are generally paid by health care providers submitting specimens; they in turn may receive payments from Medicaid and other third-party payers, including private insurers. Some states collect the fees through the sale of specimen collection kits to hospitals and birthing centers. Other states may bill hospitals, patients, physicians, Medicaid, or other third-party payers for the fee. Nationwide, newborn screening fees funded 64 percent of newborn screening program expenditures in state fiscal year 2001. (See table 4.) Thirteen state programs reported that fees were their sole source of funding in fiscal year 2001, and 19 additional states reported that fees funded at least 60 percent of their newborn screening expenditures. The average fee in the states that charged a fee was about $31, with fees ranging from $10 to $60.*

Table 4: Funding Sources for State Newborn Screening Programs, as Percentage of Nationwide Program Expenditures, State Fiscal Year 2001

Funding source	Percentage of program expenditures
Fees	64
Maternal and Child Health Services Block Grant	5
Medicaid[a]	10
Other state funds	19
Other funds[b]	2

Source: GAO Survey of State Newborn Screening Programs for Genetic and Metabolic Disorders, October 21, 2002.

Note: This table includes information for 50 states; South Dakota reported that information on state fiscal year 2001 funding sources was not available. We asked states to provide us expenditure information for laboratory and program administration/follow-up components and instructed them to include only those follow-up activities that are conducted through confirmation of diagnosis and referral for treatment. We did not ask for expenditure information for disease management and treatment services.

[a]Includes federal and state contributions.

[b]Includes, for example, the Preventive Health and Health Services Block Grant.

> *Seven state newborn screening programs identified Medicaid as a direct funding source in state fiscal year 2001. These screening programs bill the state Medicaid agency directly for laboratory services or receive a transfer of funds from the state Medicaid agency for screening services provided to Medicaid-enrolled infants. The percentage of expenditures the states reported as directly funded by Medicaid does not include Medicaid payments to hospitals for services provided to newborns.*

Other funding sources that states identified for newborn screening program expenditures include state funds and the Maternal and Child Health Services Block Grant. About half the states reported that state funds supported laboratory or program administration/follow-up expenditures. In addition, about half the states reported that they rely on the Maternal and Child Health Services Block Grant as a funding source for laboratory or program administration/follow-up expenditures. Seven states identified other funding sources, such as the Preventive Health and Health Services Block Grant.

3.14.0 If Kansas expanded its newborn screening program and chose to do so through its State laboratory, what would be the up-front costs?

If the KNSP expanded to include all of the recommended conditions included in the ACMG Report, there could be significant up-front costs depending on the procedures and technologies selected. It is also possible to defray the up-front costs through lease-purchase agreements or so-called reagent rental plans. In either of these options, costs are prorated over time and the number of tests performed so that costs can be more evenly distributed. There are, of course, somewhat increased total costs involved in the prorated plans depending on how the plans are negotiated.

In the laboratory, testing for CAH will likely require duplication of the equipment currently used for CH screening, since the testing methods are similar. Screening for biotinidase deficiency involves very little additional laboratory equipment; however, system costs will be related to decisions about detecting classical and/or variant forms of the disease. Costs for CF screening will depend on the testing algorithm selected (IRT/IRT or IRT/DNA). Assuming that the CF screening protocol is IRT/DNA, additional equipment will be needed to perform both the IRT and the DNA testing, and building modifications may be required due to additional requirements to eliminate potential contamination problems during DNA testing. The largest up-front expansion expense will likely come from the purchase of a tandem mass spectrometer, which will cost approximately $200,000. A single instrument should be adequate; however, arrangements will need to be considered for back-up capacity in the event of instrument down time for (including periodic instrument servicing and possible malfunctions). There will likely be additional expenses in renovating the laboratory space in which the machine will be housed since it requires additional air conditioning and may require noise reduction considerations to comply with Occupational Safety and Health Administration (OSHA) regulations.

It is important to have a sound accounting basis on which to calculate costs. Costs should not be limited to laboratory only, but should cover all program expenses including education, follow-up, linkages to services, counseling, and data collection (see report from the American Academy of Pediatrics Newborn Screening Task Force - *Pediatrics* 2000;106:383-427). Other program costs may include limited treatment/medical management activities if these costs are to be covered in a manner similar to the current situation. It is likely that expanded staffing will be necessary in both the laboratory and follow-up/education/evaluation parts of the KDHE screening system.

In determining costs and subsequently considering the source for funding, which may include a fee to cover some or all of the costs, it will be important to have the support of those who will likely be impacted by program expansion. This means engaging stakeholders such as health professionals, birthing facilities, insurers, Medicaid administrators, Kansas MCH and CSHCN staff, and others. In cases where an active advisory committee is functioning, this committee can serve as the venue for problem solving and advocacy among the stakeholders. The advisory committee and other stakeholders should be involved in financial and other decision-making processes so that they can feel a sense of ownership of the program and its decisions. It is important for the public and others involved in financing newborn screening to understand that newborn screening is a system and system finances MUST ultimately cover education, tracking, diagnosis, medical management, and long-term outcome studies – items sometimes overlooked in an effort to lower costs. Failure to adequately consider overall system finances and services ultimately results in lower quality of the screening program.

3.15.0 What would be the key issues to be addressed by an Advisory Group to KDHE prior to initiating NBS?

A functional advisory committee can be a powerful advisor and advocate for the program. The committee can be asked for advice on program issues that might be of importance to the medical or subspecialty community, or families, including:

- Finances (Is a fee necessary? To what extent should treatment costs be supported?)
- Computerization (Is a new system needed? How comprehensive should the system be?)
- Testing panel (Which conditions included in the newborn screening test panel)
- Testing methods (Full scan MS/MS? Total galactose or transferase? Partial biotinidase detection? IRT/IRT or IRT/DNA? Hemoglobin DNA? Second tier screening test for CAH?)
- Laboratory cutoff values/percentiles justified with data?
- Follow-up protocols and data collection elements (long-term follow-up)
- Linkage and communication with the affected infant's medical home.
- Diagnosis/disease management process.
- Legal concerns (Information to parents about other external options for screening?)
- Ethical issues (Inclusion of non-treatable conditions?)
- Public relations (interactions with the public and with the health care community).
- Education (professional and consumer).
- Outsourcing (comprehensive view of system to determine advantages and disadvantages).

Program decisions made with the advice of outside advisors should lead to stronger support for their implementation. Without participation from the community that provides program support, namely clinicians, birthing facilities, parents and families

(both affected and unaffected), and third party payers, the program faces a continuing uphill battle for its survival and effectiveness. A formal Newborn Screening Advisory Committee would likely oversee smaller working groups or subcommittees with specific interests such as for example, hemoglobinopathies, metabolic disease, endocrinopathies, parent and professional education, and community/consumer affairs. Other ad hoc or standing work groups can be formed as needed - for example for consideration of parent issues, screening for cystic fibrosis, biotinidase deficiency, or lysosomal storage diseases. Any funds needed to support the work of the Advisory Committee or its subcommittees should be included in program financing considerations.

The Review Team feels that a formal advisory system is important for all newborn screening programs. This is reinforced in other guidance about newborn screening (*Screening* 1992;1:135-47 and *Pediatrics* 2000;106:383-427). Programs have adopted various models for their advisory systems, most of which center around a central program advisory committee. The most effective advisory committees appear to have multi-disciplinary representation and usually include input from within and outside of government. An example of government programs from whom input might be important include the Medicaid Program, the Birth Defects Program, the WIC Program, the CSHCN Program, and the Newborn Hearing Screening Program. Non-government input should come from various newborn screening stakeholders, including patients and families, primary care physicians, obstetrics practitioners, midwives, the Kansas Medical Association, the local AAP Chapter, the local AAFP Chapter, the Kansas Hospital Association, nurses, nutritionists, genetic counselors, representatives from the insurance industry, community activists, subspecialty physicians with an interest in newborn screening (such as an endocrinologist, hematologist and/or metabolic disease specialist), large and small business employers, and may also include legal, ethical and religious representation. At least one State's newborn screening advisory committee includes representation from the State Legislature. It would be advisable to include lay advocates - individuals with disorders detectable by newborn screening or members of families of affected individuals. It is generally agreed that committee staffing should be provided by the program and interested follow-up, administrative, and laboratory personnel should be encouraged to attend meetings to provide technical information. However, in order to achieve the goal of obtaining outside program advice, program personnel should not have a formal role in committee deliberations or voting. It may also be useful to have an internal departmental working group that includes personnel from newborn screening program, Title V, and/or CSHCN, and staff from other related programs such as newborn hearing and birth defects, and subspecialty consultants to help guide routine program operations.

The Newborn Screening Advisory Committee should meet regularly and formally, with an appropriate agenda that includes brief descriptions of the issues to be discussed. The agenda should be available to members well in advance of committee meetings. Minutes should be a part of the formal process and should be widely and actively distributed to any interested party following each meeting. KNSP staff should assist with scheduling, agenda preparation, travel arrangements, etc. Teleconferencing is an option for some of the meetings in order to decrease costs, and all who were interviewed about the advisory committee process expressed interest in participating in such conferences.

However, there was general agreement that at least one face-to-face meeting of the committee annually was needed. The March of Dimes may be a source of outside funding to support the advisory committee if state funds are not available. Paying attention to the needs of committee members, including time and location of meetings, availability of childcare, reimbursement for travel, etc. may optimize the committee members' participation.

In whatever form the committee may take, it is essential that all members understand and agrees to its role and its rules. There must be a clearly stated mission that includes a defined committee role, e.g. to whom or to what state entity does the committee report, and process for communication with the program. Most programs have found that a strong independent chair with standing in the medical or consumer community is helpful. Some programs have used committee co-chairs to help ensure that personal agendas do not compromise the committee's effectiveness. Committee members should disclose any potential conflicts of interest. Members with conflicts should defer from being involved in decisions that might be impacted by the conflict.

3.16.0 How many states have not expanded their NBS programs? Has any state discontinued the expanded testing? Are any states considering discontinuing due to fiscal crises?

As indicated by the charts given in Section 2.9.0, only 7 programs remain without any MS/MS testing (AR, AZ, DC, KS, TN, WV, and WY), either optional or required. Of these, at least half are seriously considering its addition. Biotinidase deficiency screening is not available in 9 programs, CAH in 6, and CF in 27. In some programs counted as having screening available, the testing has not yet been required and is available as an option. These data confirm the fact that it is relatively easy to include screening for most of the metabolic, endocrine and hemoglobin conditions, but screening for CF is somewhat more complex and controversial. With the recent endorsement of newborn screening by a special working group convened by the CDC and a similar endorsement from the Cystic Fibrosis Foundation (see special supplement to Journal of Pediatrics, September 2005), programs are beginning to develop the necessary liaisons with local CF Centers, and newborn screening for CF is beginning to increase.

The only program to have discontinued expanded newborn screening is the California program, which initiated a pilot MS/MS screening program in 1999. After developing the necessary data to support expansion and establishing laboratory and follow-up protocols, the program was discontinued in 2004 because of state funding constraints. These were primarily related to the inability of the state budget to provide the increased matching funds necessary to support testing of the large numbers of Medicaid births in the State. Consumer response to the discontinuation coupled with legislative support reestablished the MS/MS expansion in 2005. This expansion included screening for CAH but expansion to include CF and biotinidase deficiency screening is still under review.

4.0.0 Other Observations from the Review Team

In addition to answering specific questions and commenting on specific issues presented by the KDHE, the Review Team also noted other items considered worthy of comment. These items reflect system issues generally addressed in the Council of Regional Networks's (CORN) description of U.S. newborn screening programs (publication in Appendix 3), and other issues considered to be important for strengthening public health newborn screening efforts.

4.1.0 Education before, during and after implementation of expanded screening

Education of primary care practitioners concerning the conditions included in expanded screening will be an important part of any expansion. The ACMG is currently completing ACTion or ACT Sheets for all conditions in its recommended panel of tests so that model information will be available for newborn screening programs to use when reporting results to the primary care practitioner. These "just in time" information sheets are designed to contain only the essential details necessary for immediate follow-up actions on the part of the clinician. Further FACT Sheets with more detailed information about the conditions are also under development and many programs already have such resources. In particular, the Massachusetts, Oregon and California programs have extensive information available. Along with the ACT Sheets, ACMG and its expert group have also developed confirmatory algorithms for use by NBS programs and their medical consultants. Because some of the medical management issues may be considered differently in different subspecialty settings, any information shared with the physician community should first be reviewed and agreed to by the subspecialty consultants in Kansas. A HRSA-funded project at the LSU Health Science Center in Shreveport produced model primary educational pamphlets for newborn screening program use aimed at parents and healthcare providers. These materials have been prepared utilizing focus groups of parents, nurses and physicians and were recently sent to all state newborn screening programs. In addition, these materials have been sent adopted and sent by the AAP and the American College of Obstetricians and Gynecologists (ACOG) to their members. The American Academy of Family Physicians (AAFP) is also planning to make the materials available to its members. Some programs have identified other educational opportunities as helpful in their educational efforts including presentations at professional meetings, publication of informational articles in the local medical journal, information on program websites, newsletters, webcasts, and videotapes.

4.2.0 Education of policy makers (e.g. Legislators).

One of the biggest challenges currently facing newborn screening programs is adequate and appropriate education of policy makers. It is essential that the KNSP be proactive in addressing the newborn screening educational needs of the governmental policy makers in Kansas. It is important for the KNSP to make sure that program and other scientific information needed for sound policy decisions is available to the policy makers needing it. There are various means of getting the message out and it is important to consider the best mechanism for accomplishing this education in a timely way. It is important that the concept of a newborn screening system be conveyed since most often the message that has been received by government officials is that newborn screening is

just an inexpensive laboratory test. There is usually little attention paid to the fact that a truly comprehensive population-based newborn screening system must serve all of the population and must provide for an appropriate and timely medical service delivery system if it is to be effective. Several programs have performed cost analyses on expanded screening for metabolic conditions and these can be accessed either through their program websites or by directly contacting the program. In particular, Wisconsin, California, Arizona and Florida have prepared such reports.

4.3.0 Program Quality Assurance

Often, quality assurance is mistakenly assumed only to apply to laboratory testing; however, many program elements outside of the laboratory can and should be monitored for quality. The quality of the entire newborn screening program (and any other public health program) should be reviewed from start to finish. For example, quality of received specimens can be judged against established criteria by monitoring unsatisfactory rates. Completeness of demographic data on the specimen collection form can be documented as can the time required to receive repeat specimens and the time from specimen collection to location and treatment of presumptive positive patients. Program coverage can be judged by comparing birth records and patients screened. Many of these parameters are best judged at the point of specimen receipt and so the screening laboratory must be aware of program needs in this respect.

Documentation of adherence to established program protocols and corrective actions taken when failures occur are essential components of the quality assurance process and should be aimed at improving overall program quality. Setting criteria for follow-up performance based on an internal operations manual, and documenting time limits for accomplishing these criteria can form the basis for such a quality assurance program. Various disorder-specific protocols for follow-up should be included in the manual. Time lines included in any of the standard operating procedures for follow-up should be realistic (as opposed to idealistic) and should include end points and corrective actions in case of failures. Periodic audits should be carried out for the complete process.

An annual review of patient treatment compliance and status provides one means for measuring treatment adequacy and quality. Physician advisor(s) who can provide professional judgment on treatment issues should be consulted to give advice on treatment reviews. The records of all quality assurance efforts should be periodically presented for review to the advisory committee. A Kansas Newborn Screening Annual Report should be considered. Excerpts from such a report in Nebraska are included in Appendix 10 as an example of how an annual report might be constructed. It should provide program visibility and be a valuable information source for those persons and organizational entities that might be interested in the program status, including its accomplishments. Further, such a report serves as an educational and promotional tool for the general public. Statistical data of program performance can be graphically displayed and can provide easily viewed summaries of program experiences. From year to year these summaries can provide a measure of program improvements. This report can be displayed on the program's website.

It is suggested that KNSP follow-up coordinator perform a systems' analysis to identify any gaps in the system and if gaps are identified, implement policies and procedures to assure closure and rectify any deficiencies. As an example, a quick review of the various birthing center websites might reveal areas of newborn screening knowledge deficiency among some birthing centers. A listing of items that form a Performance Evaluation and Assessment Scheme (PEAS) for program self-evaluation is available on the NNSGRC website and should provide a suitable template for such an evaluation. Continuous oversight and monitoring of all aspects of the newborn screening system is necessary in order to assure that quality is maintained. This oversight can best be achieved by ensuring that quality assurance is one of the job responsibilities of a particular individual in the program. Birthing facilities should be encouraged to incorporate NBS into their quality management plans with specified performance measures for those NBS components for which they are responsible. Additionally, the follow-up/medical management contracts should contain quality measures and be monitored through regular communication and periodic site visits to ensure optimal services for Kansas newborns. Reports of all external proficiency testing related to newborn screening should be shared with program administrators and the advisory committee along with documentation of any corrective actions taken.

4.4.0 Long-term follow-up (case management outcome)

Long-term follow up or management begins with the confirmation of a diagnosis and continues throughout the life of the individual. It is important for newborn screening programs to collect program evaluation data on the long-term outcome of individuals identified by screening. These data provide a mechanism for determining the effectiveness of newborn screening system and should provide information on which to base program changes and policy development. Long-term follow-up data are a critical need for most newborn screening programs. Without outcome data, it is impossible to accurately assess the program's performance, one of the core functions of public health (assessment, assurance and policy development). Not only will long-term data allow the program to assess its performance but such data can provide invaluable information about medical conditions that are rare and often not well understood.

Thus, collection and evaluation of long-term outcome data are strongly recommended as part of the follow-up responsibilities of the program, and the medical management contractors. At a minimum, sufficient information should be collected to report on the Title V NBS performance measure. Long-term outcome data can be accumulated through annual inquiries either to the primary care provider, to the consulting subspecialist (if one exists), or to the parent. Medical consultants to the programs should assist in the identification of those elements for which data should be collected. Consult NNSGRC for information on states that have developed long term follow-up processes and measures. Since long-term outcome follow-up will invariably require funding if it is to be done correctly, it is suggested that this be a consideration of any deliberations regarding the program fee. As noted in the AAP Task Force Report {[*Pediatrics* 2000;106(suppl 2):383-427] – see Executive Summary in Appendix 4}, it is strongly recommended that the entire newborn screening system be supported in such a manner that if a fee exists, it should first pay for all newborn screening system expenses

before it is absorbed into government general revenues for other programs. Table 2 provides a listing of the fees currently charged for newborn screening in the various U.S. programs. This table was constructed through telephone interviews and care should be taken not to misinterpret these data since all states use different procedures for calculating the amount of their fees. Nevertheless, the information contained in the table may be useful in comparing the fees across programs.

Table 2. Newborn Screening Program Fees

State	Births (Occurrence) In 2001	Percent Medicaid births (2000[a])	Number of screens required	Number of disorders currently mandated (1/2006)	Current Fee 1/2006	Notes
Alabama	59,766	45.0	1	14	$139.33	Two screens strongly recommended.
Alaska	9,907	52.0	1	>30	$55.00	Fee includes any repeats.
Arizona	85,757	44.0	2	8	$20.00	Separate fee for each mandated specimen.
Arkansas	36,301	43.7	1	4	$14.83	
California	528,539	42.4	1	>30	$78.00	
Colorado	67,100	32[b]	2	7	$53.25	Fee includes 2 mandated specimens (2-part form).
Connecticut	43,179	26.7	1	>30	$28.00	
Delaware	11,360	41.0	2	29	$64.00	Fee includes 2 mandated specimens and any repeats.
District of Columbia	15,037	28[b]	1	7	No Fee	
Florida	205,991	44.0	1	5	$15.00	
Georgia	134,402	44.0	1	10	No Fee	
Hawaii	17,127	25.0	1	>30	$47.00	
Idaho	20,161	34.2	1	>30	$23.00	$46 for double kits if screening occurs prior to 48 hrs.
Illinois	181,086	37.2	1	>30	$47.00	
Indiana	86,710	42.0	1	>30	$62.50	Includes $32.50 laboratory surcharge and all repeats.
Iowa	37,756	23.0	1	>30	$56.00	Fee includes any repeats.
Kansas	39,052	12[b]	1	4	No Fee	
Kentucky	53,227	38.8	1	4	$14.50	
Louisiana	65,620	41.0	1	5	$18.00	Fee expected to increase to $40.00 later in 2005.
Maine	13,567	20[b]	1	9	$44.00	
Maryland	68,663	29.0	1	>30	$42.50	Fee includes repeats; 2 screens strongly recommended.
Massachusetts	82,237	24.2	1	10	$54.75	
Michigan	132,159	27.7	1	11	$55.72	Fee includes any repeats.
Minnesota	67,428	31.3	1	>30	$61.00	
Mississippi	41,145	53.7	1	40	$70.00	
Missouri	76,690	39.0	1	14	$25.00	
Montana	10,935	40.0	1	4	$39.34	
Nebraska	25,107	28.8	1	6	$30.75	
Nevada	31,007	27.6	2	>30	$60.00	Fee includes 2 mandated specimens (2-part form).
New Hampshire	14,055	20.8	1	6	$18.00	Fee includes hemoglobinopathies when requested.
New Jersey	112,639	23[b]	1	20	$71.00	
New Mexico	26,808	49.6	2	6	$32.00	Fee includes 2 mandated specimens (2-part form).
New York	255,029	41.1	1	>30	No Fee	
North Carolina	119,132	40.5	1	26	$10.00	
North Dakota	8,839	28.0	1	29	$36.00	
Ohio	152,033	33.1	1	30	$33.75	
Oklahoma	48,895	46.0	1	7	$75.59	Fee includes hearing screening.
Oregon	46,200	32.2	2	26	$54.00	Fee includes 2 mandated specimens (2 -part form). Extra single forms are $27.
Pennsylvania	143,957	25.0	1	6	No Fee	Many hospitals offer extra tests for fee. Fees vary.
Rhode Island	13,319	35.4	1	9	$59.00	
South Carolina	53,255	47.0	1	30	$42.00	
South Dakota	10,784	32.8	1	3	$18.53	Fee does not include hemoglobinopathies if requested.
Tennessee	83,521	37.7	1	>30	$47.50	
Texas	370,482	45.1	2	5	$19.50	Separate fee for each mandated specimen.
Utah	49,041	25.8	2	4	$31.00	Fee includes 2 mandated specimens (2-part form).
Vermont	6,149	23.0	1	21	$33.30	
Virginia	96,535	22.7	1	9	$32.00	
Washington	79,078	42.5	1	9	$60.90	Fee includes repeats; 2 screens strongly recommended.
West Virginia	21,000	55.2	1	4	No Fee	
Wisconsin	68,006	35.5	1	26	$65.50	$30.00 laboratory surcharge included in fee.
Wyoming	5,758	38.0	1	7	$45.00	Fee implemented for first time August 1, 2004.
TOTAL	4,031,531	39[b] (Nationally)				

(a) From Kaiser State Health Facts Online, http://www.statehealthfacts.kff.org.
(b) 2000 Medicaid statistics unavailable so statistics are taken from Kaiser Commission on Medicaid and the Uninsured, 1995.

Long-term outcome data on the impact of newborn screening are scarce. Particular emphasis has been placed on PKU since dietary compliance for women with PKU is especially important during pregnancy, and since other adverse affects of non-compliance with dietary therapy have been demonstrated in persons not maintained on treatment for life (the reader is referred to: *Report of the NIH Consensus Development Conference on Phenylketonuria: Screening and Management, October 16-18, 2000.* National Institutes of Health, Washington, D.C., February 2001). Apart from selected research studies on some of the other disorders included in newborn screening programs, particularly for congenital hypothyroidism, most newborn screening programs have not maintained long-term follow-up data. A recent report on newborn screening outcomes in Georgia (Van Naarden BK, Yeargin-Allsopp M, Schendel D, Fernhoff P. *Long-term developmental outcomes of children identified through a newborn screening program with a metabolic or endocrine disorder: a population-based approach.* J Pediatr;143:236-42) supports the importance of maintaining these types of data. Wherever possible, outcome data should be maintained as long as possible in order to ensure availability of, and compliance with, prescribed medical treatment programs, and to provide the valuable program evaluation data needed to justify the continuation and expansion of newborn screening activities. The process of obtaining and maintaining long-term information has been made more complex by the national focus on privacy and recent passage of federal and state privacy legislations, including the Health Insurance Portability and Accountability Act (HIPAA). Nonetheless, long-term outcome data are essential for program evaluation and provide a mechanism for documenting that affected children are receiving needed services in a timely way.

Some programs have found it productive to use their advisory groups as proponents and contributors to long-term outcome tracking. In some cases, it may be useful to analyze the data for research purposes and the consultants should be apprised of this opportunity. It is important that any new conditions have long-term outcome data collection included in their implementation. It is much easier to begin collecting data prospectively with new disorders than to establish it for disorders currently in the program, and for which there is little enthusiasm for documenting successful outcome (having already been established in most people's minds, whether or not it has been established to the satisfaction of the policy makers). Some of the data that might be collected long-term include:

- Age at definitive diagnosis and initiation of treatment for each disorder.
- Demographic and clinical profiles of the patients under treatment.
- Mortality and morbidity measures for each disorder.
- Measures of compliance with treatment protocols.
- Measures of long-term outcome and functionality of patients (schooling, employment, psycho-social adaptation, reproductive success, etc.).
- Costs associated with treatment.

4.5.0 Computerization

The system currently in place for computerized specimen management in the KNSP laboratory is an internally developed and maintained system. Patient management records are part of the CSHCN computer system. With expansion, additional computerization or computer software enhancement will be needed. Computer considerations should include a comprehensive system that will include laboratory specimen management, result management, patient tracking, long-term data management, etc. Care should be taken in final specifications to incorporate the experiences of other users into an improved system meeting the specific program needs in Kansas. Additionally, consideration should be given to data integration, automated data downloads from birthing facilities and 24 hour access to result reports either through secure on line reporting mechanisms or alternative systems such as voice response. The information system should be constructed to anticipate the increasing use of electronic health records in the community. Reporting to the national database using an automated process should also be considered.

National Data -

Since 1988, national newborn screening data have been collected and these data have expanded over the years until today there is a comprehensive real time On Line data reporting system for newborn screening information (NNSIS) (http://www2.uthscsa.edu/nnsis). In order for a newborn screening program to maintain its quality, efficiency and effectiveness, the data accumulated within the program must continually be analyzed and compared to historic data and data from other programs. Without valid program data concerning such basic items, it is difficult to accurately assess program quality. Further, these data are needed for both the first and second specimen so that the usefulness of the repeat specimens can be continually assessed. Evaluation of racial/ethnic services requires that racial/ethnic information on cases detected be maintained and validated through birth records. Some commercial systems now allow these data to be downloaded automatically to the NNSIS and this should be a consideration in the computerized system currently being planned.

Program evaluation was addressed by the AAP Newborn Screening Task Force [*Pediatrics* 2000; 106 (suppl 2): p. 413] in the following way:

Ideally, the information obtained by a newborn screening program would allow the description of:

- *The number and percent of children*
  - *adequately screened,*
  - *with appropriate follow-up,*
  - *with false-positive and false-negative results,*
  - *with specific diagnoses, and*
  - *with appropriate care.*
- *The time between the newborn screen and the initiation of treatment.*

- *The long-term improvement in health status occurring as a result of screening, follow-up, diagnosis, and treatment.*
- *The number of children diagnosed with a condition missed by the screening programs and, where possible, an assessment of the reasons they were missed.*
- *The number and percentage of children lost to follow-up.*
- *Defining reporting procedures (e.g., what reports will be made, who will receive them).*
- *Ensuring commitment to maintaining systems.*
- *Ensuring that procedures for maintaining, transmitting, analyzing, and disseminating data conform to ethical guidelines and legal standards.*

Data Integration -

Little has been mentioned about newborn screening for hearing loss in this report, even though it is included in the ACMG newborn screening discussions. Because of the similarities in newborn hearing screening (NHS) and traditional newborn dried blood spot (DBS) screening, many states have developed consolidated hearing and blood spot screening as a more efficient way of providing newborn health services. Some states have linked or integrated the information from these screening programs to other child health programs such as immunization and birth defects registries as well as to vital records. While comprehensive newborn screening data consolidation may not have been seen as a need within the individual programs, data integration is a growing national concern as a means of more efficiently serving the patient. Not only are there discussions about sharing information among public health programs but discussions about how best to electronically share information between the public health and clinical domains are becoming more commonplace.

Access to public health information, such as screening results and service encounter information, would likely be more useful if it were readily available at the point of care, i.e. the child's medical home. Data integration efforts are being actively supported nationally by grant initiatives at both the CDC and HRSA. The Review Team strongly encourages consideration of appropriate software and hardware capabilities in any new purchases that would allow data integration activities at some future time. Integrated information systems are already being developed in public health departments in an effort to minimize data duplication and to provide basic client information to multiple programs from a single information source. Ultimately, it is envisioned that secure patient information will become available to healthcare providers through the Internet or downloadable electronic health records using desktop computers, portable laptop computers or other portable personal information devices. A few state public health departments, including Rhode Island and Utah, have already developed the capacity for such information sharing. Not only can public health information be made readily available to health care providers, but programs can also receive status updates from clinicians. Currently at least one foreign program is already experimenting with downloadable information through

automated text messaging to cellular telephones.

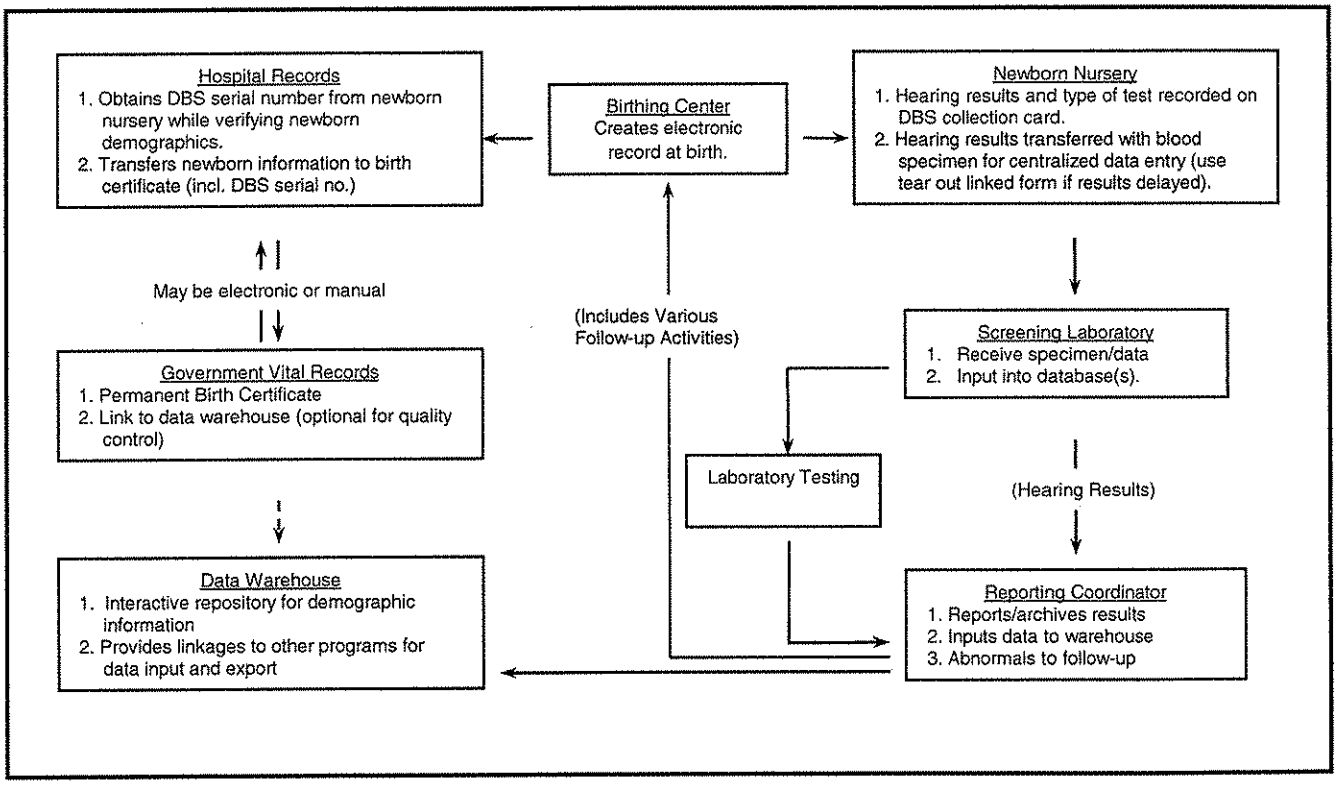
Useful patient information for children includes immunization status and information from other public programs, from which the child may eventually receive services such as the CSHCN Program, Women, Infants, and Children (WIC) Program or others. Additionally, in order to ensure full population coverage in DBS and NHS and to validate the demographic reported on each patient, data integration with vital records is desirable. Most of the systems currently in development contain a central repository of certain data elements that are consistent among the different programs, such as the basic patient demographic information - name, date of birth, sex, race/ethnicity, etc., and allow data sharing with other program-specific data systems. An integrated information system using these data may be envisioned as a wheel and spoke arrangement. In the center of the wheel is the central repository of general patient demographic information with spokes branching out to program specific data or information. If the design is well thought out and planned, then the demographic information can be specific and comprehensive enough to meet the needs of virtually every program and can result in a comprehensive integrated public health record for an individual child, i.e. a child health profile. In such a system, patient demographic information can be input by the program having the first patient encounter. Subsequent programs would first inquire to see if the information were available and current before duplicating the data input. Program specific data would be maintained in a secure fashion accessible only to those designated users who have a right and a need to know.

As an example, the patient demographic information required for NHS follow-up is similar to that required for routine newborn DBS follow-up. The minimal data elements suggested for DBS newborn screening, and collected on the DBS collection card of every newborn, are specified in a national standard (now in its fourth revision) and are limited to the essential data elements needed for identifying patients considered at risk as a result of screening (see CLSI/NCCLS LA4-A4). Already captured in most DBS databases are: infant's name, address, phone number, physician of record, physician's phone number, etc. The same essential data are required for follow-up of newborns with a congenital hearing loss. It is logical that data systems should be able to take advantage of data availability in order to diminish the amount of data entry required for each patient. (see Figure 2). Indeed, many programs have found that a single data entry system can efficiently be used for data capture for both the DBS and NHS programs, thus avoiding duplication and reducing overall costs of data entry. Sometimes this is done by placing hearing results on the DBS form being submitted to the State and sometimes through electronic birth certificates or other mechanisms. Currently in Kansas, the two databases appear to be totally independent, contain duplicate demographic information, and there is only limited connectivity to other patient information such as birth records.

By limiting the universal information captured on patients to the essential elements needed to identify and locate the patient, the amount of data entered into the central repository can be streamlined. Case specific information on the relatively small number of patients with abnormal DBS or NHS test results can be accessed

later as part of the follow-up process. Limiting the case specific data in this way has been found to add efficiency to the data collection/data entry task by leaving non-critical information to be obtained later on the less than 1% of patients for whom it is needed. Thus, for example, additional data elements specific to hearing loss or metabolic conditions are often recorded in a program-specific case management database (or other appropriate file) in a process similar to what currently occurs in the two separate KDHE newborn screening programs. In cases where a screening program may wish to monitor risk factors for all patients, additional data elements could be added to the DBS form, for example, and entered along with the routine demographic information. These data could then be transferred into a separate program-specific database. However, care must be taken to ensure that the information anticipated from additional data of this type is valid and useful, since data entry expenses will be increased by any addition of information.

Figure 2. Diagram of newborn screening data flow using the warehousing concept and linkages with vital records as a means of ensuring that all newborns receive both a newborn screen and a birth certificate.



Timely information available from DBS and NHS programs could also provide demographic information useful for populating or validating birth certificate data, as shown in Figure 1 (left-hand side). If newborn screening data cannot be used to populate the birth certificate database for technical or logistical reasons, they can still be valuable as a quality control check to ensure that birth certificates exist for each newborn receiving a newborn screening test. Reverse validation may also be beneficial in assuring that each recorded birth has received an appropriate newborn screening test (although programs should be sensitive to the fact that birth certificate information is not collected to be used punitively). Because most of the DBS

conditions require earlier identification in order to ensure optimal outcomes, a quicker match is needed if the birth certificate is to be useful for ensuring 100% screening coverage. While this delay may not be the result of the matching process, an alternative to the current practice is the use of the DBS serial number. This unique identifier (described in CLSI/NCCLS LA4-A4) can provide a simpler, unique and readily available identifier to link birth certificates, NHS and other child health and vital records programs together as long as a field for this number is included in each linking database.

As newborn screening expands to include additional conditions in Kansas, data management needs will increase. It may be useful to consider the feasibility of using the DBS computer system to capture NHS data (or the reverse) in order to assist in meeting some of these data needs. Both newborn screens (NHS and DBS) occur before the newborn leaves the nursery and both programs utilize essentially the same patient demographic information. Submission of limited hearing screening data with the newborn screening form provides one way of quickly obtaining hearing information on each and every newborn in the state. Integration of these data into a centralized follow-up/service management system can be facilitated by a combined data approach and can aid in the timely follow-up of those newborns who need additional services. Data integration through combined NHS and DBS data elements on the DBS screening form has already been accomplished in over 15 states and the "lessons learned" in these experiences may prove useful in any considerations of this type in Kansas.

A truly comprehensive linked or integrated newborn health information system would theoretically include mechanisms for integrating initial patient information from any program that may have the data available, whether or not it originated in a newborn screening encounter (see Figure 3). Thus, for example, if a child was to be given an immunization, an inquiry of the central repository should indicate whether or not there was basic demographic information available, and additionally whether or not there was an immunization history. If demographic data were missing, then they would be input at that time and would be available for future inquiries, whether or not the inquiry originated with the immunization program.

Consideration of this type of linked or integrated system will involve data and application integration. Building upon the successes of various data systems within KDHE is a logical progression towards improved patient care and should be strongly considered. Useful references discussing current public health information integration activities may be found in Appendix 11 of this report and also in a special issue of the *Journal of Public Health Management and Practice*, November 2004 Supplement. An additional resource is the Public Health Informatics Institute (http://www.phii.org), currently funded by HRSA to support state efforts in child health information integration activities. The Robert Woods Johnson Foundation has a new program to fund grants in support of state and local public health agency participation in heath information activities (http://www.informationlinks.org).

Figure 3. Diagram showing data flow into and out of a data warehouse, with particular attention to interactions with newborn screening, birth certificates, immunization registries, and birth defects registries.